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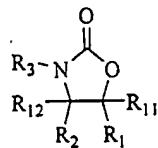
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(71) Applicant (<i>for all designated States except US</i>): VERSICOR, INC. [US/US]; 34790 Ardentech Court, Fremont, CA 94555 (US).		
(72) Inventors; and (75) Inventors/Applicants (<i>for US only</i>): GORDEEV, Mikhail F. [RU/US]; 15267 Hesperian Boulevard, San Leandro, CA 94578 (US). LUEHR, Gary, W. [US/US]; 33252 Palomino Common, Fremont, CA 94555-1522 (US). PATEL, Dinesh, V. [US/US]; 45109 Cougar Circle, Fremont, CA 94539		Published <i>With international search report.</i>
(54) Title: OXAZOLIDINONE COMBINATORIAL LIBRARIES, COMPOSITIONS AND METHODS OF PREPARATION		
(57) Abstract		
<p>Oxazolidinones and methods for their synthesis are provided. Also provided are combinatorial libraries comprising oxazolidinones, and methods to prepare the libraries. Further provided are methods of making biologically active oxazolidinones as well as pharmaceutically acceptable compositions comprising the oxazolidinones. The methods of library preparation include the attachment of oxazolidinones to a solid support. The methods of compound preparation in one embodiment involve the reaction of an iminophosphorane with a carbonyl containing polymeric support.</p>		

CLAIMS

What is claimed is:

1. A method for the solid phase synthesis of oxazolidinones, comprising the steps of:
 - 5 a) attaching an olefin to a solid support;
 - b) oxidizing the olefin to provide an epoxide functionality;
 - c) opening the epoxide with an amine to form an amino alcohol; and
 - d) cyclizing the amino alcohol using a phosgene equivalent.
2. The method according to claim 1, where the olefin is an allylic amine or
10 allylamine.
3. The method according to claim 1, where the amine is an amino acid, or an aromatic amine.
4. A method for the synthesis of oxazolidinone combinatorial libraries, comprising the steps of:
 - 15 a) attaching an olefin group to an array of solid supports;
 - b) oxidizing the individual olefin groups to provide an array of solid support bound epoxides; and
 - c) opening the epoxide with an amine to form an amino alcohol; and
 - d) cyclizing the amino alcohol using a phosgene equivalent.
- 20 5. The method according to claim 4, where the olefin is an allylic amine, or allylamine.
6. The method according to claim 4, where the amine units are amino acids or aromatic amines.
7. An oxazolidinone combinatorial library, where the oxazolidinones
25 comprising the library are of the following structure:



1a

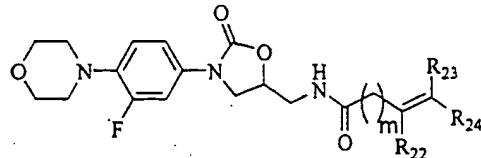
where R₁ is selected from the group consisting of alkyl, heteroalkyl, aryl and heteroaryl, R₂ is selected from the group consisting of hydrogen, alkyl, heteroalkyl, aryl and heteroaryl, R₃ is selected from the group consisting of hydrogen, alkyl, heteroalkyl, aryl and heteroaryl, R₁₁ is selected from the group consisting of hydrogen, alkyl, heteroalkyl, aryl and heteroaryl, and R₁₂ is selected from the group consisting of hydrogen, alkyl, heteroalkyl, aryl and heteroaryl.

8. The combinatorial library according to claim 7, where R₃ is selected from the group consisting of aryl and heteroaryl, and further where the aryl and heteroaryl groups are the aryl and heteroaryl groups attached to the amines of Table 2 and Figures 29, 10 30, and 31.

9. The combinatorial library according to claim 7, where R₃ is a heteroaryl group selected from the group consisting of a pyridyl group, a thiienylphenyl group, an oxazolyl group, a pyrrolyl group, and a morpholinofluorophenyl group.

10. An antimicrobial compound where the compound is of the structure:

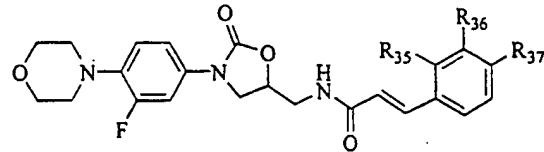
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where m is 0, 1, 2 or 3, and where R₂₂, R₂₃ and R₂₄ are independently selected from the group consisting of hydrogen, alkyl, heteroalkyl, aryl and heteroaryl.

11. The antimicrobial compound according to claim 10, where m is 0, and 20 where R₂₂ and R₂₃ are hydrogen, and where R₂₄ is an aryl group.

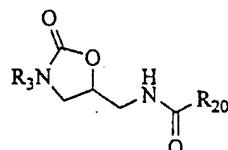
12. The antimicrobial compound according to claim 11, where the compound is of the structure:



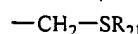
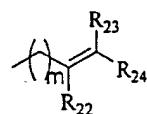
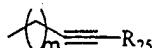
where R₃₅, R₃₆ and R₃₇ are independently selected from the group consisting of hydrogen, electron withdrawing group, alkyl, heteroalkyl, aryl and heteroaryl.

13. An antimicrobial compound, where the compound has the following structure:

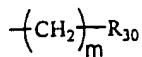
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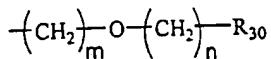
where R₃ is selected from the group consisting of aryl and heteroaryl, and where R₂₀ is selected from the group consisting of structures A, B, C, I, J and K

**A****B****C**

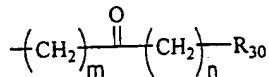
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I



J



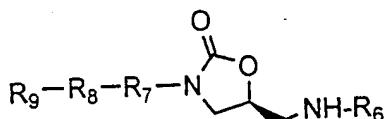
K

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wherein m is 0, 1, 2 or 3, and wherein n is 0, 1, 2 or 3, and wherein R₂₁ is selected from the group consisting of alkyl, heteroalkyl, aryl and heteroaryl, and where R₂₂, R₂₃ and R₂₄ are independently selected from the group consisting of hydrogen, alkyl, heteroalkyl, aryl and heteroaryl, and where R₂₅ is selected from the group consisting of hydrogen, alkyl, heteroalkyl, aryl and heteroaryl, and where R₃₀ is selected from the group consisting of alkyl, heteroalkyl, aryl and heteroaryl.

10

14. A compound of formula 2c:



15

2c

wherein:

R₆ is acyl or sulfonyl;

R₇ is aryl or heteroaryl;

R₈ is C₁-C₇ alkyl, NR, O, S, C(=O)NR, NRC(=O), C(=O), C(=O)O, OC(=O), S(=O), SO₂, SO₂NR, NRSO₂, NRCONR', or (CH₂)_nO, wherein n = 0-6, and wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl; and

and

5 R₉ is hydrogen, OH, alkyl, aryl, heteroalkyl, or heteroaryl.

15. The compound of claim 14 wherein:

R₆ is C(=O)R, wherein R is H, alkyl, or aryl;

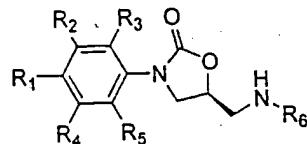
R₇ is aryl;

10 R₈ is NH(C=O) or NR'(C=O), where R' is H, alkyl, or aryl; and

R₉ is hydrogen, pyridinyl, thiazolyl, benzothiazolyl, isothiazolyl, quinolinyl, 1,3,4-triazolyl, or 1,3,4-thiadiazolyl.

16. A compound of the structure 1b:

15



1b

wherein R₂, R₃, R₄ and R₅ are, independently, hydrogen, alkyl, heteroalkyl, heteroaryl or an electron withdrawing group; R₆ is acyl or sulfonyl; and, R₇ is one of the following functional groups: C(O)NR₈, wherein R₇ and R₈ are, independently, hydrogen, alkyl, heteroalkyl, aryl or heteroaryl; C(O)OR₉, wherein R₉ is hydrogen, alkyl, heteroalkyl, aryl or heteroaryl; C(O)R₁₀, wherein R₁₀ is hydrogen, alkyl, heteroalkyl, aryl or heteroaryl; S(O)₂R₁₁, wherein R₁₁ is hydrogen, alkyl, heteroalkyl, aryl or heteroaryl; SR₁₁, wherein R₁₁ is hydrogen, alkyl, heteroalkyl, aryl or heteroaryl; S(O)R₁₁, wherein R₁₁ is hydrogen, alkyl, heteroalkyl, aryl or heteroaryl; NR₁₂R₁₃, wherein R₁₂ and R₁₃ are, independently, hydrogen, acyl, sulfonyl, alkyl, heteroalkyl, aryl or heteroaryl; 2-oxazolyl, wherein R₁₄ is at the 4-position and R₁₅ is at the 5-position of the oxazolyl, and wherein R₁₄

and R₁₅ are, independently, hydrogen, alkyl, heteroalkyl, aryl, heteroaryl or an electron withdrawing group; 2-aminothiazolyl, wherein R₁₆ is at the 4-position and R₁₇ is at the 5-position of the thiazole, and wherein R₁₆ and R₁₇, are, independently, hydrogen, alkyl, heteroalkyl, aryl, heteroaryl or an electron withdrawing group; and, CH₂NR₁₈R₁₉, wherein R₁₈ and R₁₉, are, independently, hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, acyl or sulfonyl.

- 5 17. A combinatorial library of compounds according to claim 16.
18. A compound of claim 16, wherein R₁ is C(O)NR₈, C(O)OR₉, C(O)R₁₀, SR₁₁, S(O)₂R₁₁, S(O)R₁₁ or NR₁₂R₁₃.
- 10 19. A compound according to claim 16, wherein R₁ is C(O)NR₈.
20. A compound according to claim 16, wherein R₁ is C(O)OR₉.
21. A compound according to claim 16, wherein R₁ is C(O)R₁₀.
22. A compound according to claim 16, wherein R₁ is SR₁₁.
- 15 23. A compound according to claim 16, wherein R₁ is NR_x(C=O)R_y, wherein R_x and R_y are independently hydrogen, alkyl, heteroalkyl, aryl, or heteroaryl.
24. A compound according to claim 16, wherein R₁ is NR_x(SO₂)R_y, wherein R_x and R_y are independently hydrogen, alkyl, heteroalkyl, aryl, or heteroaryl with the proviso that R_y is not H.
- 25 25. A compound according to claim 16, wherein R₁ is NR₁₂R₁₃.
26. A compound according to claim 16, wherein R₁ is 2-oxazolyl, wherein R₁₄ is at the 4-position and R₁₅ is at the 5-position of the oxazole group.
27. A compound according to claim 16, wherein R₁ is 2-aminothiazolyl, wherein R₁₆ is at the 4-position and R₁₇ is at the 5-position of the aminothiazolyl group.
- 25 28. A compound according to claim 16, wherein R₁ is CH₂NR₁₈R₁₉.
29. A compound according to claim 18; wherein R₃, R₄ and R₅ are hydrogen.
30. A compound according to claim 29, wherein R₂ is fluorine.
31. A compound according to claim 30, wherein, R₆ is C(O)CH₃.
32. A compound according to claim 31, wherein R₁ is C(O)NR₈R₈ and R₇ is hydrogen.
- 30 33. A compound according to claim 32, wherein R₈ is heteroaryl.
34. A biologically active oxazolidinone derived from a combinatorial library

according to claim 17.

35. A compound according to claim 19, wherein R₃, R₄ and R₅ are hydrogen.
36. A compound according to claim 26, wherein R₃, R₄ and R₅ are hydrogen.
37. A compound according to claim 27, wherein R₃, R₄ and R₅ are hydrogen.
- 5 38. A compound according to claim 35, wherein R₂ is fluorine.
39. A compound according to claim 36, wherein R₂ is fluorine.
40. A compound according to claim 37, wherein R₂ is fluorine.
41. A compound according to claim 38, wherein R₆ is C(O)CH₃, and NR₇R₈ is NH(5'-(5-aminopyridine-2-yl)thiopyridine-3'-yl) or NH(pyridine-3-yl).
- 10 42. A compound according to claim 38, wherein R₆ is C(O)CH₂SMe, and NR₇R₈ is NH(5-chloropyridine-3-yl).
43. A compound according to claim 38, wherein R₆ is C(O)CHCH(pyridine-3-yl), and R₇R₈ is NH(5-chloropyridine-3-yl).
- 15 44. A method of preparing the combinatorial libraries according to claim 17, comprising the steps of:
 - a) attaching a plurality of aryl oxazolidinones to a plurality of solid supports;
 - b) functionalizing the 4-position of the aryl groups of the attached oxazolidinones; and, optionally,
 - 20 c) removing the oxazolidinones from the solid supports.
45. The method according to claim 44, wherein the aryl oxazolidinone is attached to a solid support through the reaction of an iminophosphorane with a carbonyl containing resin to form an imine.
- 25 46. The method according to claim 44, wherein the aryl oxazolidinone is attached to a solid support through the reaction of an amine with a carbonyl containing resin to form an imine.
47. The method according to claim 45, wherein the attachment further comprises the step of reducing the imine.
- 30 48. The method according to claim 46, wherein the attachment further comprises the step of reducing the imine.
49. A method of synthesizing the compounds according to claim 16, wherein

the method comprises the steps of:

- a) providing an iminophosphorane;
- b) mixing the iminophosphorane with a resin that comprises carbonyl groups to form an imine intermediate; and,
- 5 c) reducing the imine intermediate to afford a compound attached to the resin through an amine linkage.

50. A method according to claim 49, wherein the iminophosphorane is provided from an azide that is reacted with a phosphine.

51. A method according to claim 49, wherein the iminophosphorane is provided from an amine that is reacted with a (trisubstituted)phosphine dihalide.

52. A method according to claim 49, wherein the resin comprising carbonyl groups is of the structure



1c

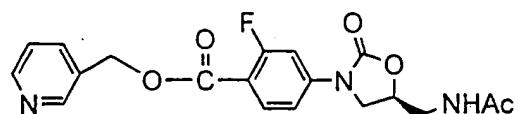
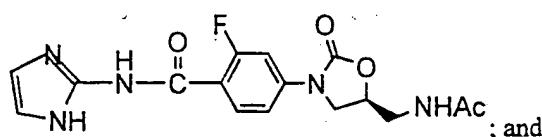
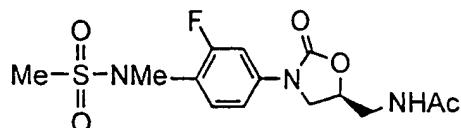
15 wherein R₂₃ is hydrogen, alkyl, aryl, O-alkyl or O-aryl; R₂₄ is hydrogen, CH₃O or NO₂; R₂₅ is (CH₂)_nCONH, wherein n is an integer between 1 and about 5; and, the filled circle is a polymeric support.

53. A method according to claim 52, wherein R₂₃ is hydrogen, R₂₄ is CH₃O, R₂₅ is (CH₂)₃CONH, and the filled circle is Tentagel, (cross-linked)polystyrene, (cross-linked)polyethyleneglycol or polyethyleneglycol-polystyrene compositions.

20 54. A method of synthesizing a compound according to claim 16, wherein the method comprises the steps of:

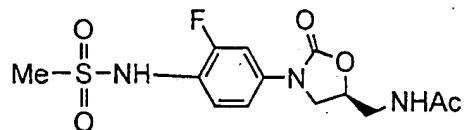
- a) reacting an amine with a resin that comprises carbonyl groups to form an imine intermediate; and
- 25 b) reducing the imine intermediate to afford a compound attached to the resin through an amine linkage.

55. The compound of claim 14 selected from the group consisting of

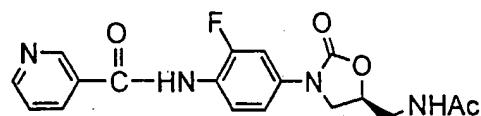
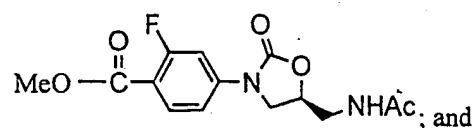


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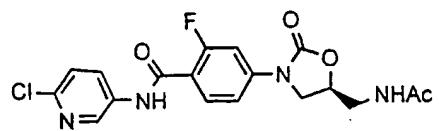
56. The compound of claim 14 selected from the group consisting of



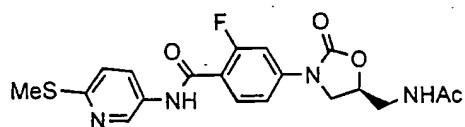
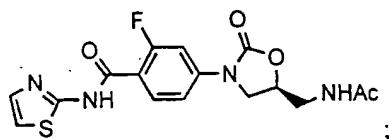
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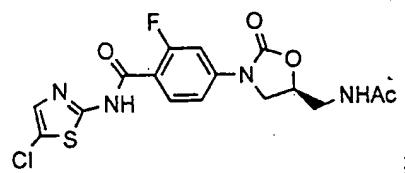
57. The compound of claim 14 selected from the group consisting of



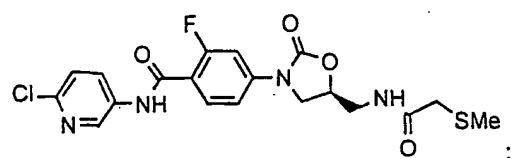
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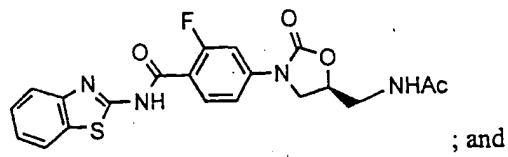
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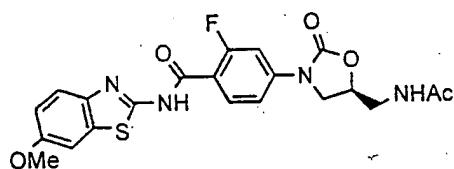
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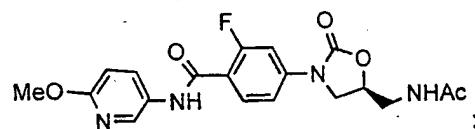


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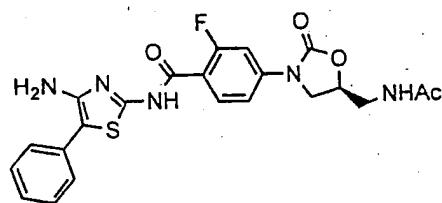


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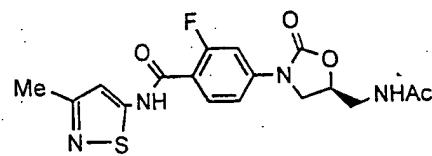
58. The compound of claim 14 selected from the group consisting of



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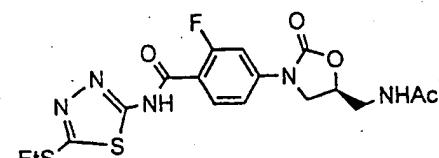


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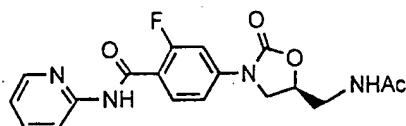
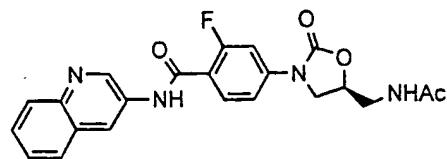


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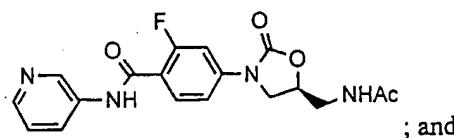
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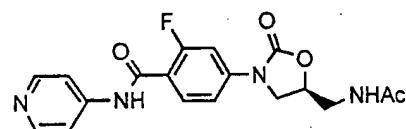
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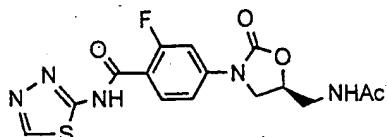


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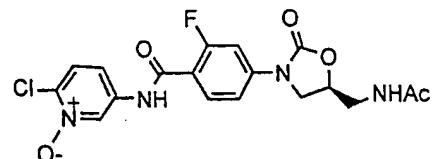


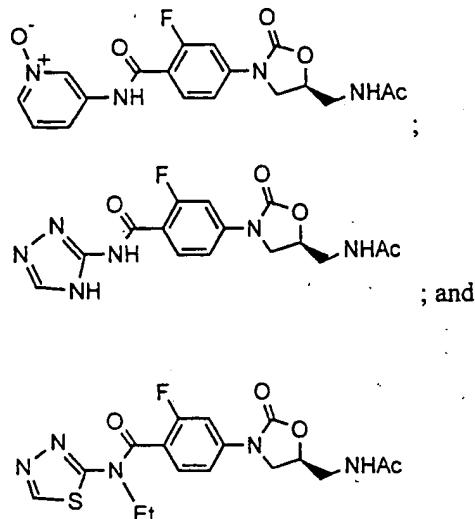
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59. The compound of claim 14 selected from the group consisting of



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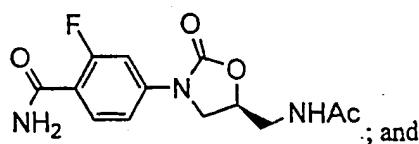
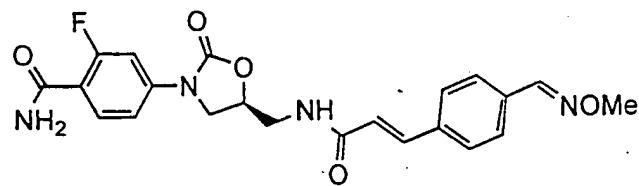
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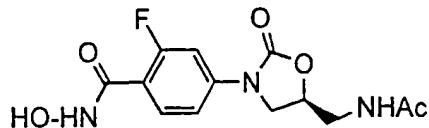
60. The compound of claim 14 wherein:

R₆ is C(=O)R, wherein R is H, alkyl, heteroalkyl, aryl or heteroaryl;R₇ is aryl;10 R₈ is NH(C=O); andR₉ is hydrogen or OH.

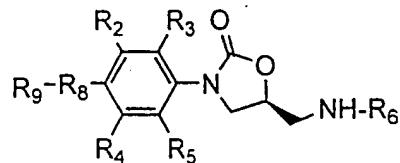
61. The compound of claim 14 wherein the compound is selected from the group consisting of:

15





5 62. A compound of formula 3c



3c

10

wherein:

R₂, R₃, R₄ and R₅ are, independently, hydrogen, alkyl, heteroalkyl, heteroaryl or an electron withdrawing group;

R₆ is acyl or sulfonyl;

15 R₈ is C₁-C₇ alkyl, NR, O, S, C(=O)NR, NRC(=O), C(=O), C(=O)O, OC(=O),

S(=O), SO₂, SO₂NR, NRSO₂, NRCONR', or (CH₂)_nO, wherein n = 0-6, and wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl; and

R₉ is alkyl, aryl, heteroalkyl, or heteroaryl.

20 63. The compound of claim 62, wherein

R₆ is C(=O)CH₃;

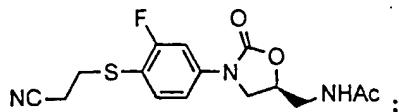
R₇ is aryl;

R₈ is S; and

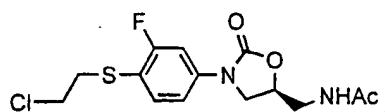
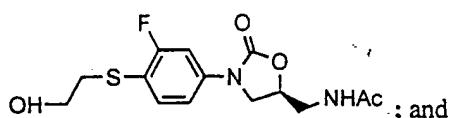
R₉ is heteroalkyl.

25

64. The compound of claim 62, wherein the compound is selected from the group consisting of

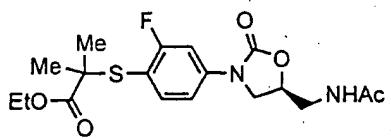


5

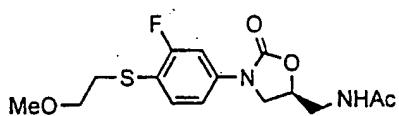
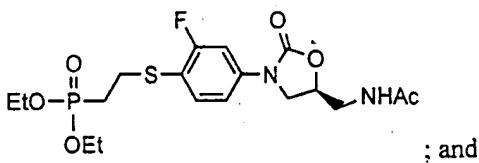
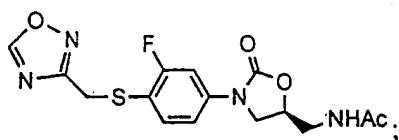


10

65. The compound of claim 62, wherein the compound is selected from the group consisting of

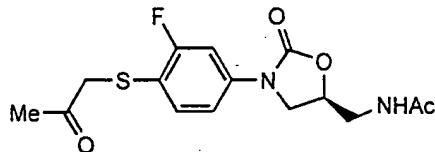


15

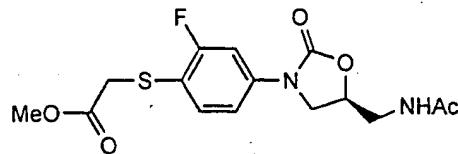


66. The compound of claim 62, wherein the compound is selected from the group consisting of

5

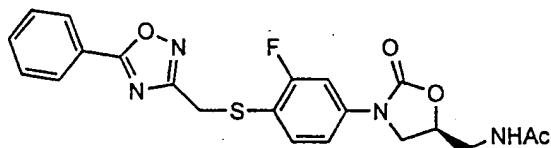


;



; and

10



67. The compound of claim 62 wherein:

R₆ is C(=O)CH₃;

15

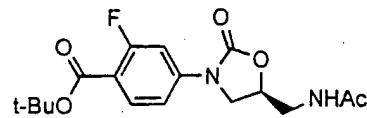
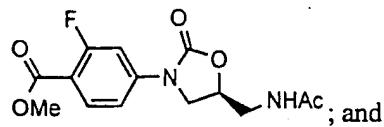
R₇ is aryl;

R₈ is OC(=O); and

R₉ is alkyl.

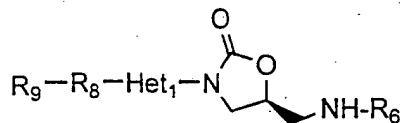
68. The compound of claim 62 selected from the group consisting of:

20



5

69. A compound of formula 4c:



10

4c

wherein:

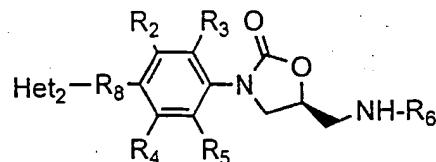
R₆ is acyl or sulfonyl;Het₁ is heteroaryl;R₈ is C₁-C₇ alkyl, NR, O, S, C(=O)NR, C(=O)NOR, NRC(=O), C(=O), C(=O)O,15 OC(=O), S(=O), SO₂, SO₂NR, NRSO₂, NRCONR', or (CH₂)_nO, wherein n = 0-6, and

wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl; and

R₉ is alkyl, aryl, heteroalkyl, or heteroaryl.

70. A compound of formula 5c:

20



5c

wherein:

R₂, R₃, R₄ and R₅ are, independently, hydrogen, alkyl, heteroalkyl, heteroaryl or an electron withdrawing group;

R₆ is acyl or sulfonyl;

R₈ is C₁-C₇ alkyl, NR, O, S, C(=O)NR, NRC(=O), C(=O)NOR C(=O), C(=O)O, OC(=O), S(=O), SO₂, SO₂NR, NRSO₂, NRCONR', or (CH₂)_nO, wherein n = 0-6, and wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl; and

Het₂ is a heterocyclic group.

71. The compound of claim 70, wherein

R₆ is C(=O)CH₃;

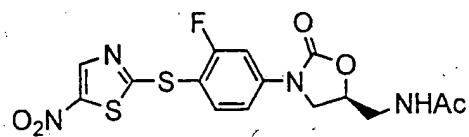
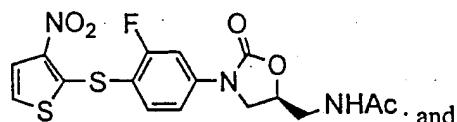
R₇ is aryl;

R₈ is S; and

Het₂ is a thiénylphenyl or thiazolyl group.

72. The compound of claim 70 selected from the group consisting of:

20



73. The compound of claim 70 wherein:

R₆ is C(=O)CH₃;

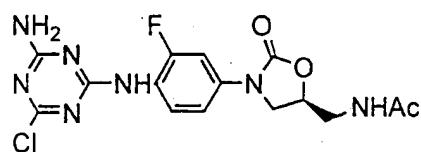
R₇ is aryl;

R₈ is NH; and

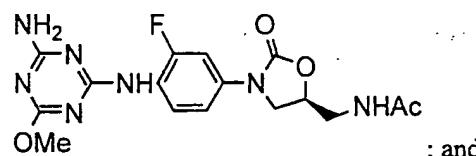
5 Het₂ is 1,3,5-triazinyl.

74. The compound of claim 70 selected from the group consisting of

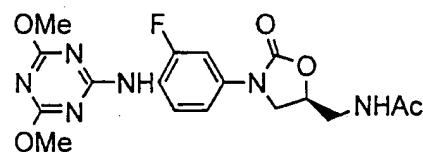
10



;

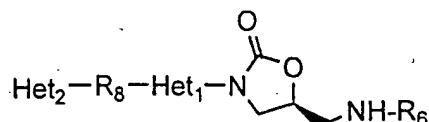


; and



15

75. A compound of formula 6c:



6c

20

wherein:

R₆ is acyl or sulfonyl;

R₈ is C₁-C₇ alkyl, NR, O, S, C(=O)NR, NRC(=O), C(=O)NOR C(=O),

C(=O)O, OC(=O), S(=O), SO₂, SO₂NR, NRSO₂, NRCONR', or (CH₂)_nO,

5

wherein n = 0-6, and wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl;

Het₁ is heteroaryl; and

Het₂ is a heterocyclic group.

10

76. The compound of claim 75 wherein

Het₁ is selected from the group consisting of thienylphenyl,

thiazolyl, 1,3,4-thiadiazolyl, pyridinyl, pyrimidinyl, phenyl and

fluorophenyl; and

15

Het₂ is selected from the group consisting of oxazolyl, isoxazolyl,

1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,3-oxadiazolyl, thienylphenyl,

thiazolyl, isothiazolyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,3,4-

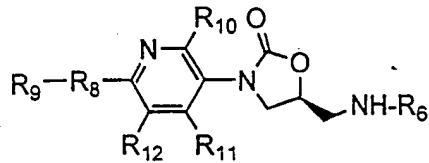
thiadiazolyl, pyrrolyl, imidazolyl, pyrazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl,

1,2,3-triazinyl, 1,2,4-triazinyl, tetrazolyl, pyridinyl, pyrazinyl, pyrimidinyl,

pyridazinyl, 1,2,4-triazinyl, 1,3,5-triazinyl, and 1,2,4,5-tetrazinyl.

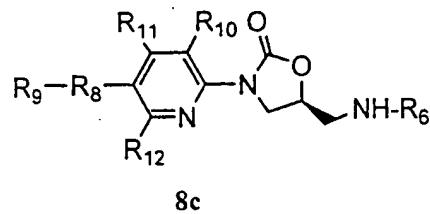
20

77. A compound of formulas 7c or 8c:



7c

25



wherein:

5 R₆ is acyl or sulfonyl;

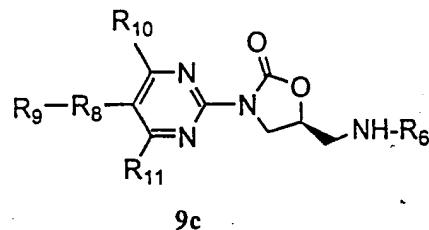
R₈ is C₁-C₇ alkyl, NR, O, S, C(=O)NR, C(=O)NOR, NRC(=O), C(=O), C(=O)O, OC(=O), S(=O), SO₂, SO₂NR, NRSO₂, NRCONR', or (CH₂)_nO, wherein n = 0-6, and wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl;

R₉ is alkyl, aryl, heteroalkyl, or heteroaryl; and

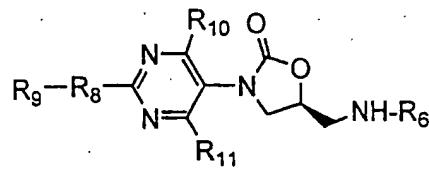
10 R₁₀, R₁₁ and R₁₂ are independently hydrogen, alkyl, aryl, heteroalkyl, electron withdrawing group, F, Cl, CN, NO₂, NR''R''', OR'', SR'', S(=O)R'', SO₂R'', C(=O)R'', C(=O)OR'', OC(=O)R'', C(=O)NR''R''', N(R'')C(=O)R''', or N-oxide group in the pyridine nuclei, wherein R'' and R''' are independently H, alkyl, heteroalkyl, aryl or heteroaryl.

15

78. A compound of formula 9c or 10c:



20



wherein:

R₆ is acyl or sulfonyl;

R₈ is C₁-C₇ alkyl, NR, O, S, C(=O)NR, C(=O)NOR, NRC(=O), C(=O), C(=O)O,

5 OC(=O), S(=O), SO₂, SO₂NR, NRSO₂, NRCONR', or (CH₂)_nO, where n = 0-6, and

where R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl;

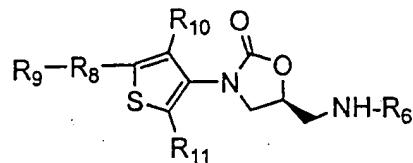
R₉ is alkyl, aryl, heteroalkyl, or heteroaryl; and

10 R₁₀ and R₁₁ are independently hydrogen, alkyl, aryl, heteroalkyl, electron withdrawing group, F, Cl, CN, NO₂, NR''R''', OR'', SR'', S(=O)R'', SO₂R'', C(=O)R'',

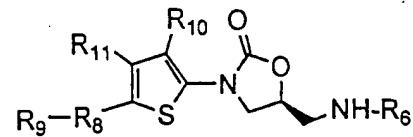
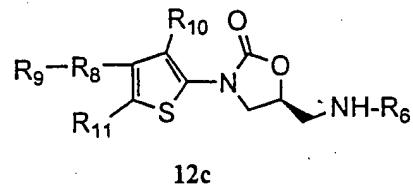
C(=O)OR'', OC(=O)R'', C(=O)NR''R''', N(R'')C(=O)R''', or N-oxide group in the pyrimidine nuclei, wherein R' and R''' are independently H, alkyl, heteroalkyl, aryl or heteroaryl.

79. A compound of formula 11c, 12c or 13c:

15



20



13c

wherein:

R₆ is acyl or sulfonyl;

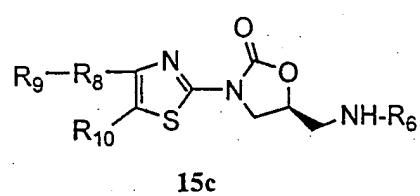
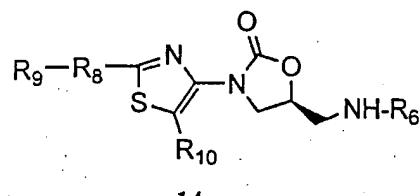
R₈ is C₁-C₇ alkyl, NR, O, S, C(=O)NR, C(=O)NOR, NRC(=O), C(=O), C(=O)O, OC(=O), S(=O), SO₂, SO₂NR, NRSO₂, NRCONR', or (CH₂)_nO, wherein n = 0-6, and wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl;

R₉ is alkyl, aryl, heteroalkyl, or heteroaryl; and

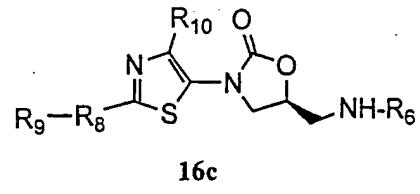
R₁₀ and R₁₁ are independently hydrogen, alkyl, aryl, heteroalkyl, electron withdrawing group, F, Cl, CN, NO₂, NR''R''', OR'', SR'', S(=O)R'', SO₂R'', C(=O)R'', C(=O)OR'', OC(=O)R'', C(=O)NR''R''', or N(R'')C(=O)R''', wherein R'' and R''' are independently H, alkyl, heteroalkyl, aryl or heteroaryl.

80. A compound of formula 14c, 15c or 16c:

15



20



wherein:

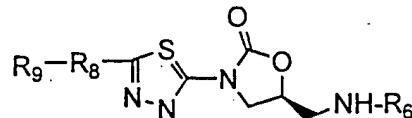
R₆ is acyl or sulfonyl;

R₈ is C₁-C₇ alkyl, NR, O, S, C(=O)NR, C(=O)NOR, NRC(=O), C(=O), C(=O)O, OC(=O), S(=O), SO₂, SO₂NR, NRSO₂, NRCONR', or (CH₂)_nO, wherein n = 0-6), and
5 wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl;

R₉ is alkyl, aryl, heteroalkyl, or heteroaryl; and

R₁₀ is hydrogen, alkyl, aryl, heteroalkyl, electron withdrawing group, F, Cl, CN, NO₂, NR''R''', OR'', SR'', S(=O)R'', SO₂R'', C(=O)R'', C(=O)OR'', OC(=O)R'', C(=O)NR''R''', or N(R'')C(=O)R''', where R'' and R''' are independently H, alkyl, 10 heteroalkyl, aryl or heteroaryl.

81. A compound of formula 17c:



15

17c

wherein:

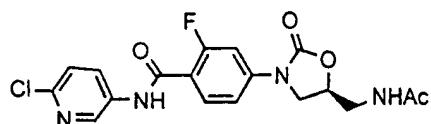
R₆ is acyl or sulfonyl;

R₈ is C₁-C₇ alkyl, NR, O, S, C(=O)NR, C(=O)NOR, NRC(=O), C(=O), C(=O)O, OC(=O), S(=O), SO₂, SO₂NR, NRSO₂, NRCONR', or (CH₂)_nO, where n = 0-6, and
20 wherein R and R' are independently H, alkyl, heteroalkyl, aryl or heteroaryl; and

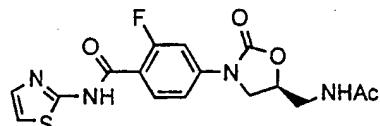
R₉ is alkyl, aryl, heteroalkyl, or heteroaryl..

82. A composition for the treatment or prevention of an infectious disorder
25 comprising an effective amount of a compound of claim 14 and a pharmaceutically acceptable carrier.

83. The composition of claim 82 wherein the compound is

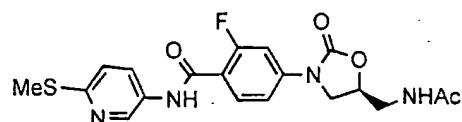


84. The composition of claim 82 wherein the compound is



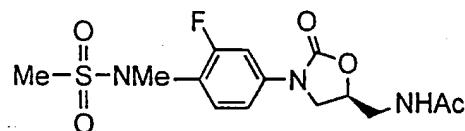
5

85. The composition of claim 82 wherein the compound is



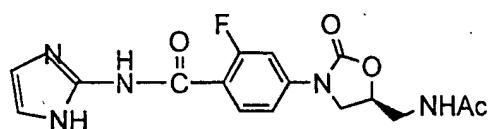
10

86. The composition of claim 82 wherein the compound is



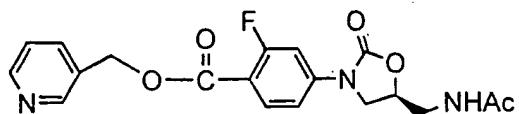
87. The composition of claim 82 wherein the compound is

15



88. The composition of claim 82 wherein the compound is

20

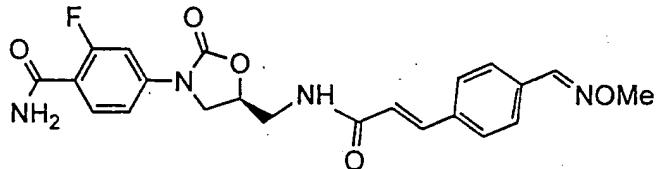


89. A composition for the treatment or prevention of an infectious disorder comprising an effective amount of a compound of claim 55 and a pharmaceutically acceptable carrier.

90. A composition for the treatment or prevention of an infectious disorder comprising an effective amount of a compound of claim 57 and a pharmaceutically acceptable carrier.

10

91. The composition of claim 82, wherein the compound is



15

92. A composition for the treatment or prevention of an infectious disorder comprising an effective amount of a compound of claim 61 and a pharmaceutically acceptable carrier.

20

93. A composition for the treatment or prevention of an infectious disorder comprising an effective amount of a compound of claim 64 and a pharmaceutically acceptable carrier.

25

94. A composition for the treatment or prevention of an infectious disorder comprising an effective amount of a compound of claim 72 and a pharmaceutically acceptable carrier.

95. A method of treating or preventing an infectious disorder in a human or other animal subject, comprising administering to the subject an effective amount of a compound of claim 14.

5 96. A method of treating or preventing an infectious disorder in a human or other animal subject, comprising administering to the subject an effective amount of a compound of claim 55.

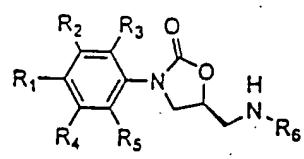
10 97. A method of treating or preventing an infectious disorder in a human or other animal subject, comprising administering to the subject an effective amount of a compound of claim 57.

15 98. A method of treating or preventing an infectious disorder in a human or other animal subject, comprising administering to the subject an effective amount of a compound of claim 61.

99. A method of treating or preventing an infectious disorder in a human or other animal subject, comprising administering to the subject an effective amount of a compound of claim 64.

20 100. A method of treating or preventing an infectious disorder in a human or other animal subject, comprising administering to the subject an effective amount of a compound of claim 72.

1 / 50



1b

FIGURE 1

2 / 50

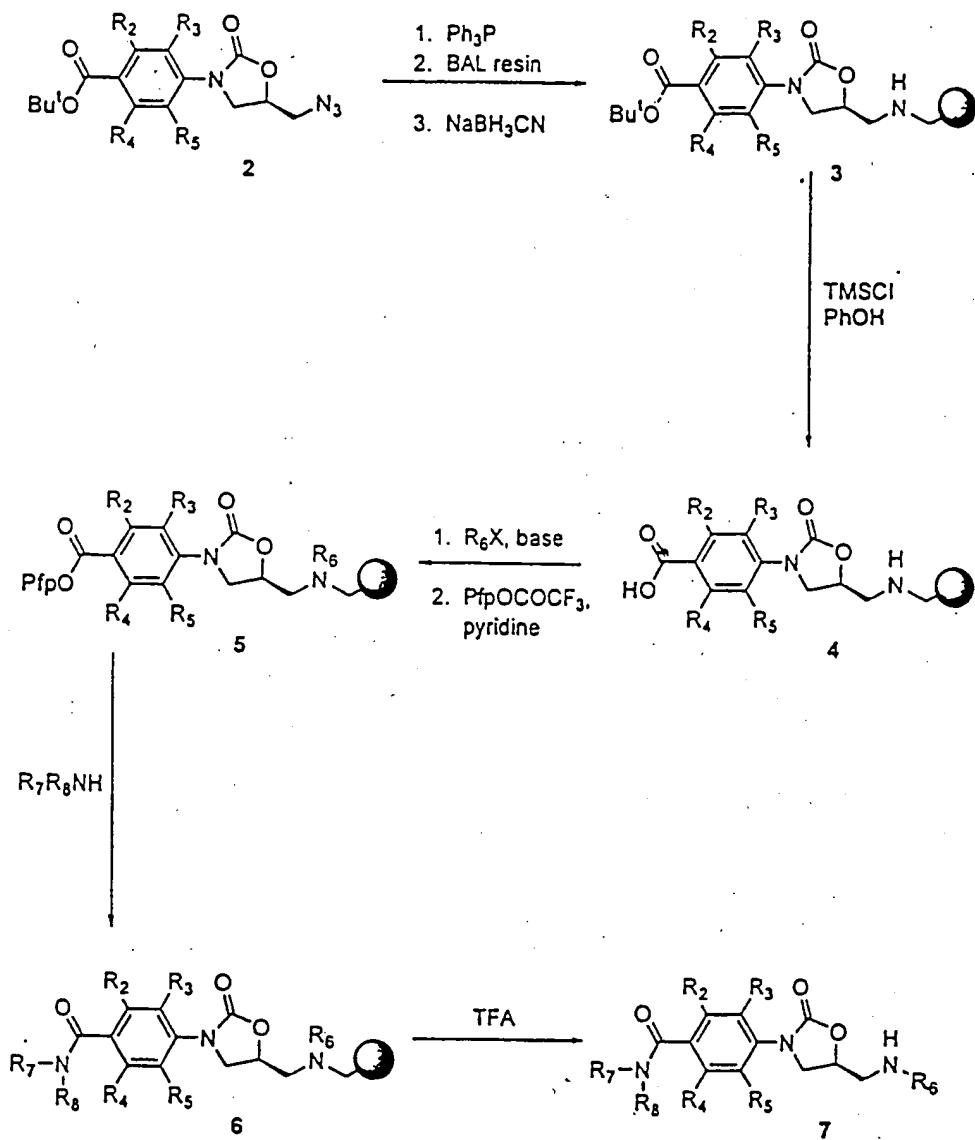


FIGURE 2

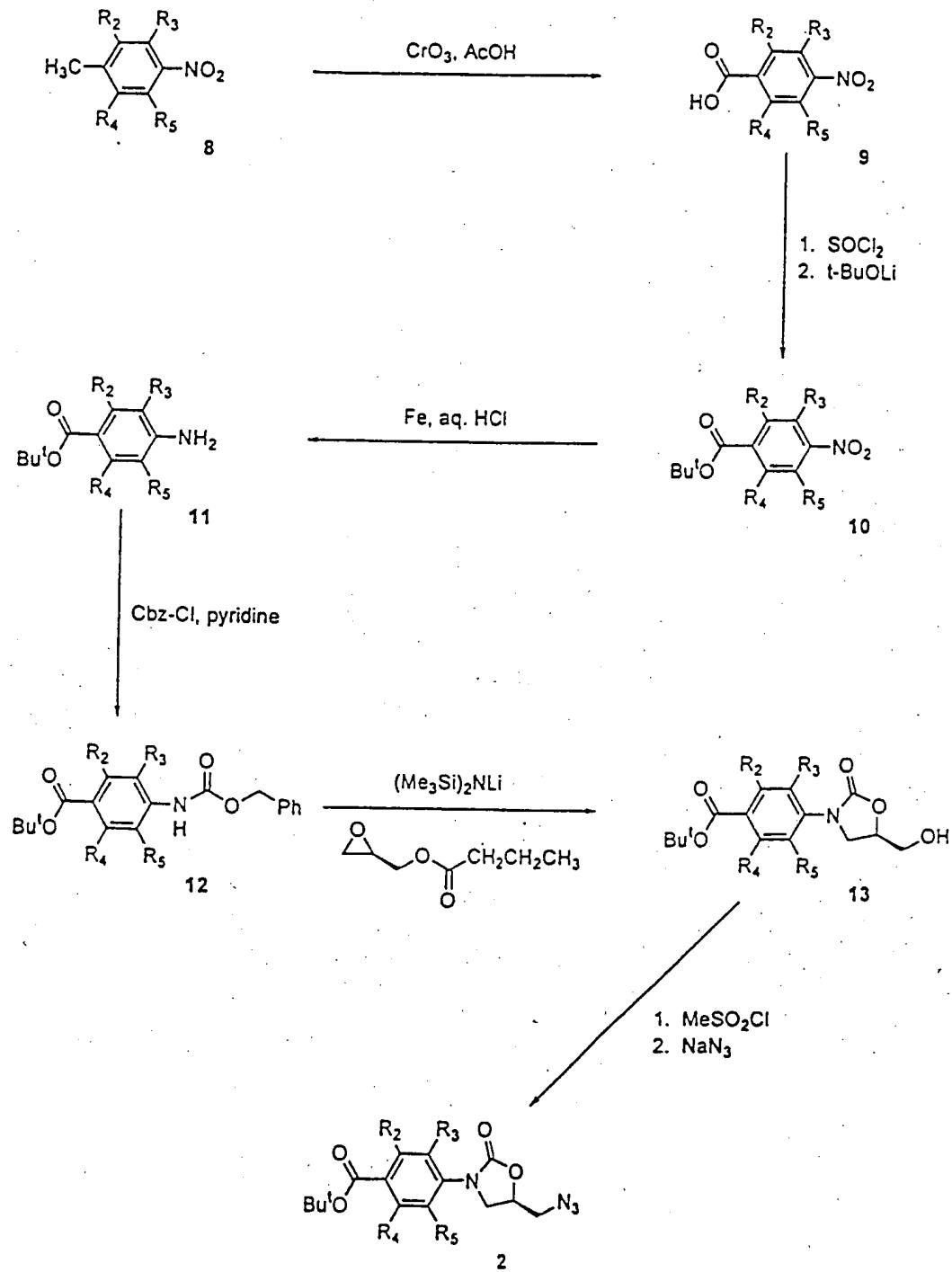


FIGURE 3

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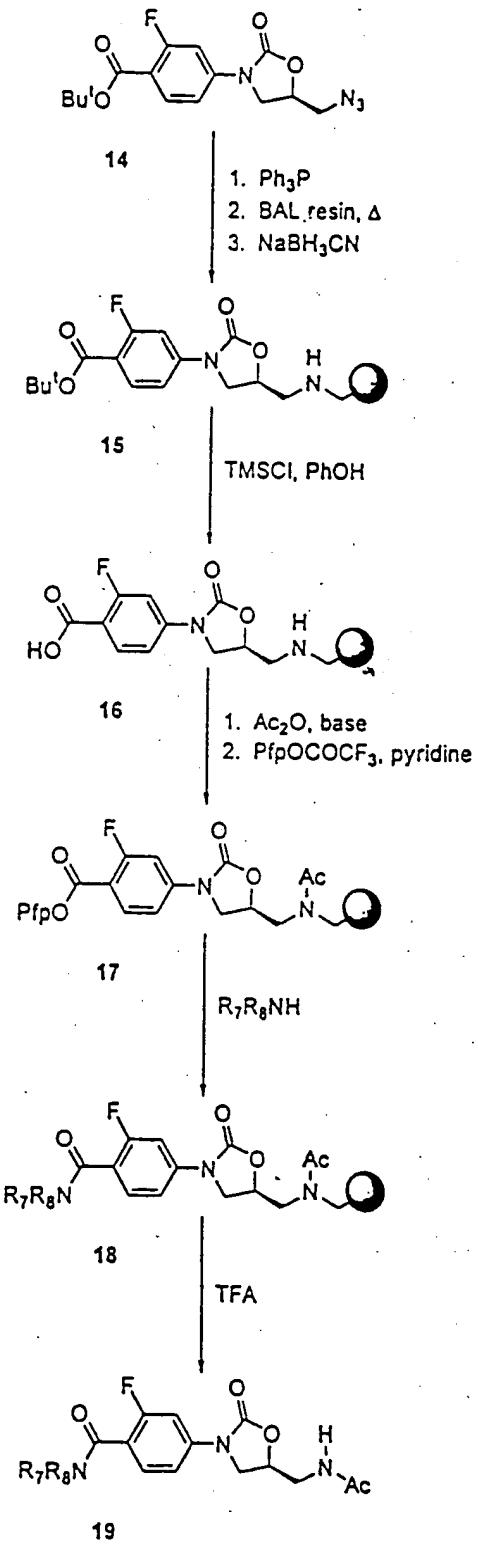


FIGURE 4

5 / 50

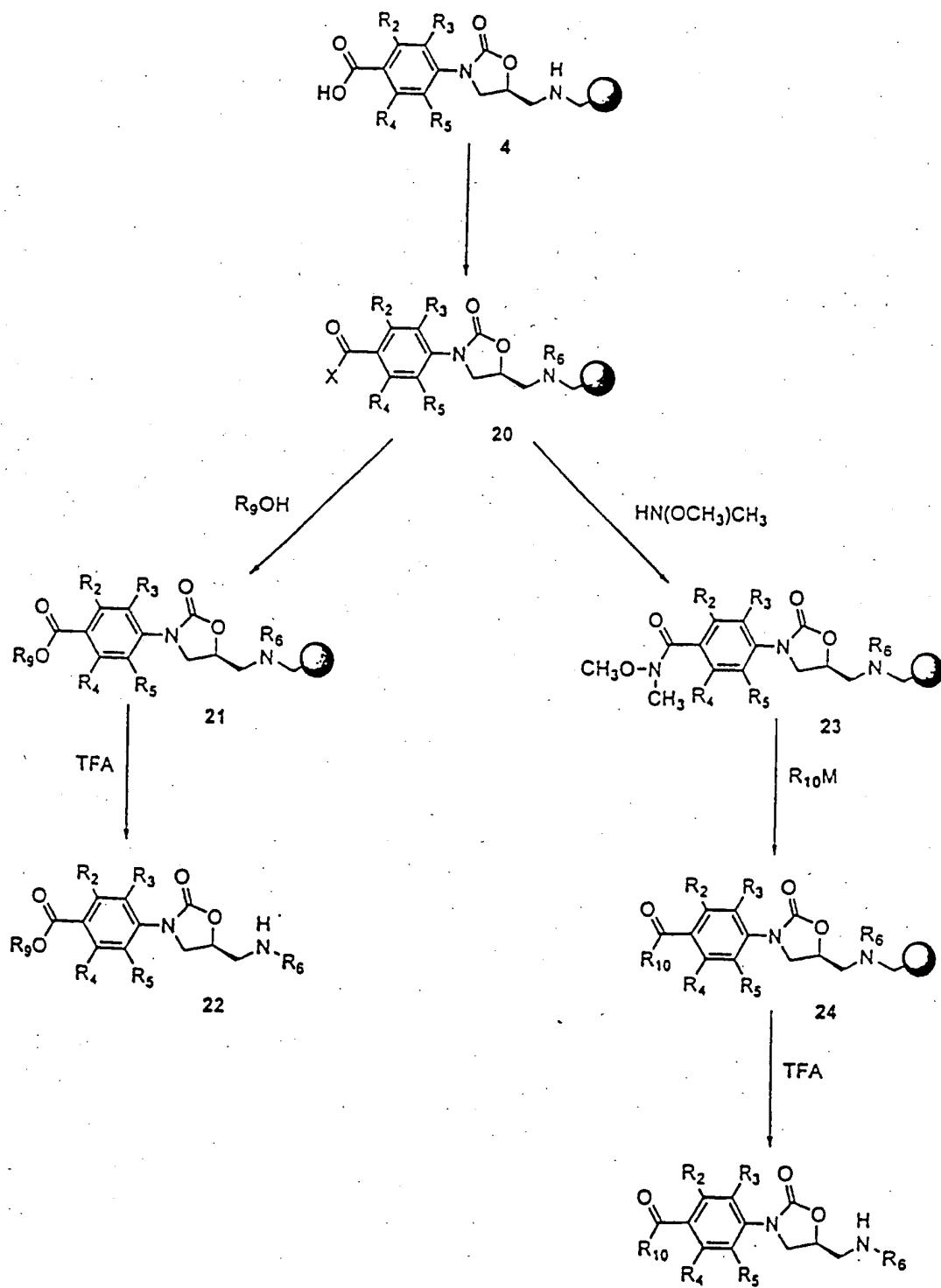
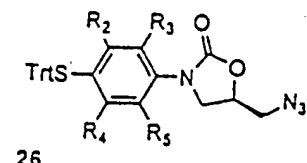


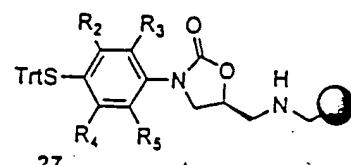
FIGURE 5

25

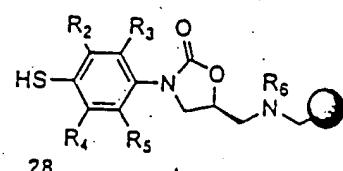
6 / 50



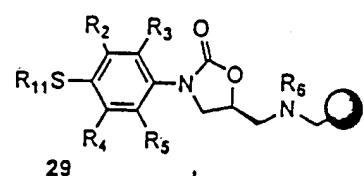
1. Ph_3P
 2. BAL resin
 3. NaBH_3CN



1. R_6X , base
 2. deprotection



R_{11}X , base



TFA

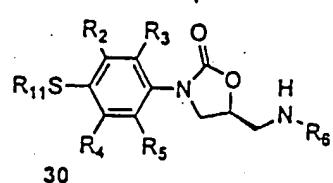


FIGURE 6

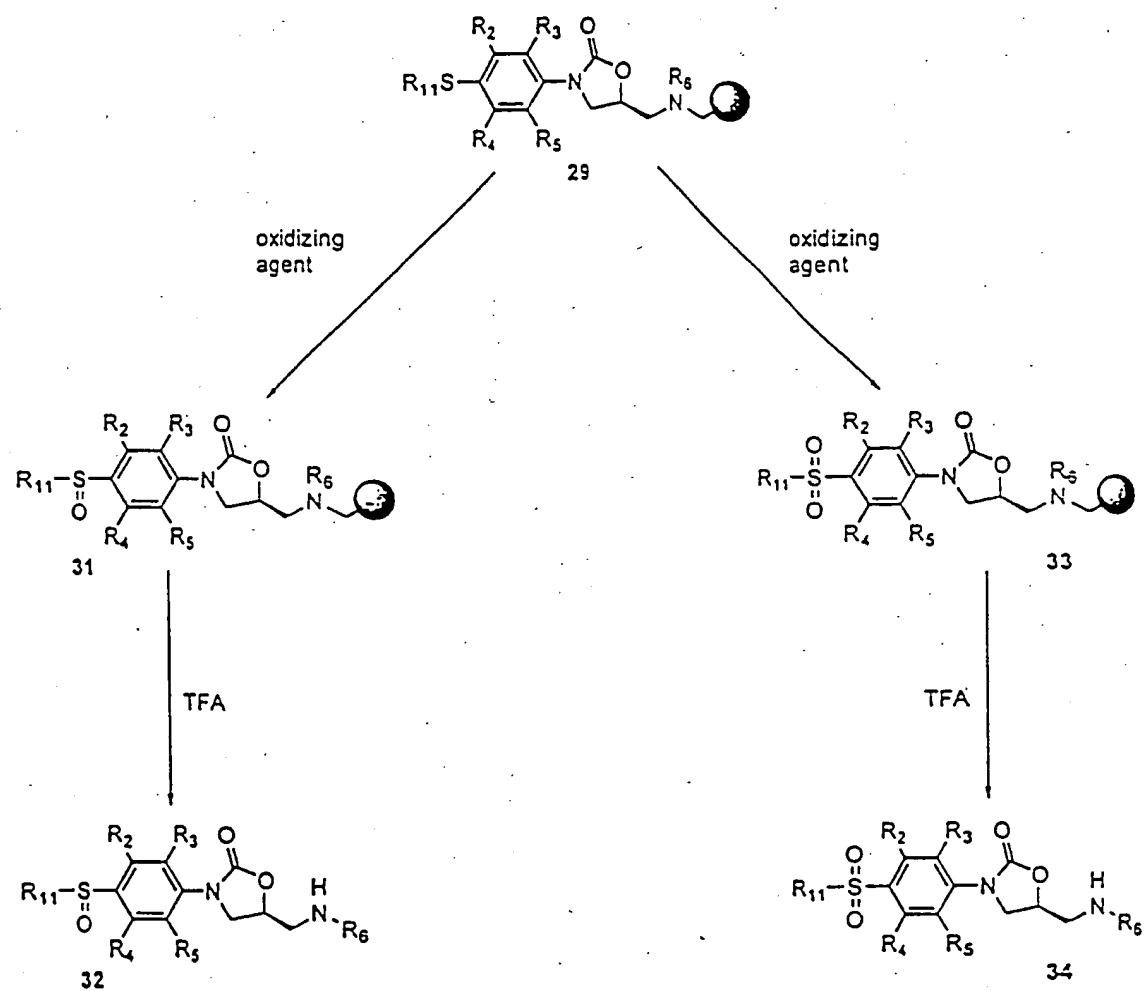


FIGURE 7

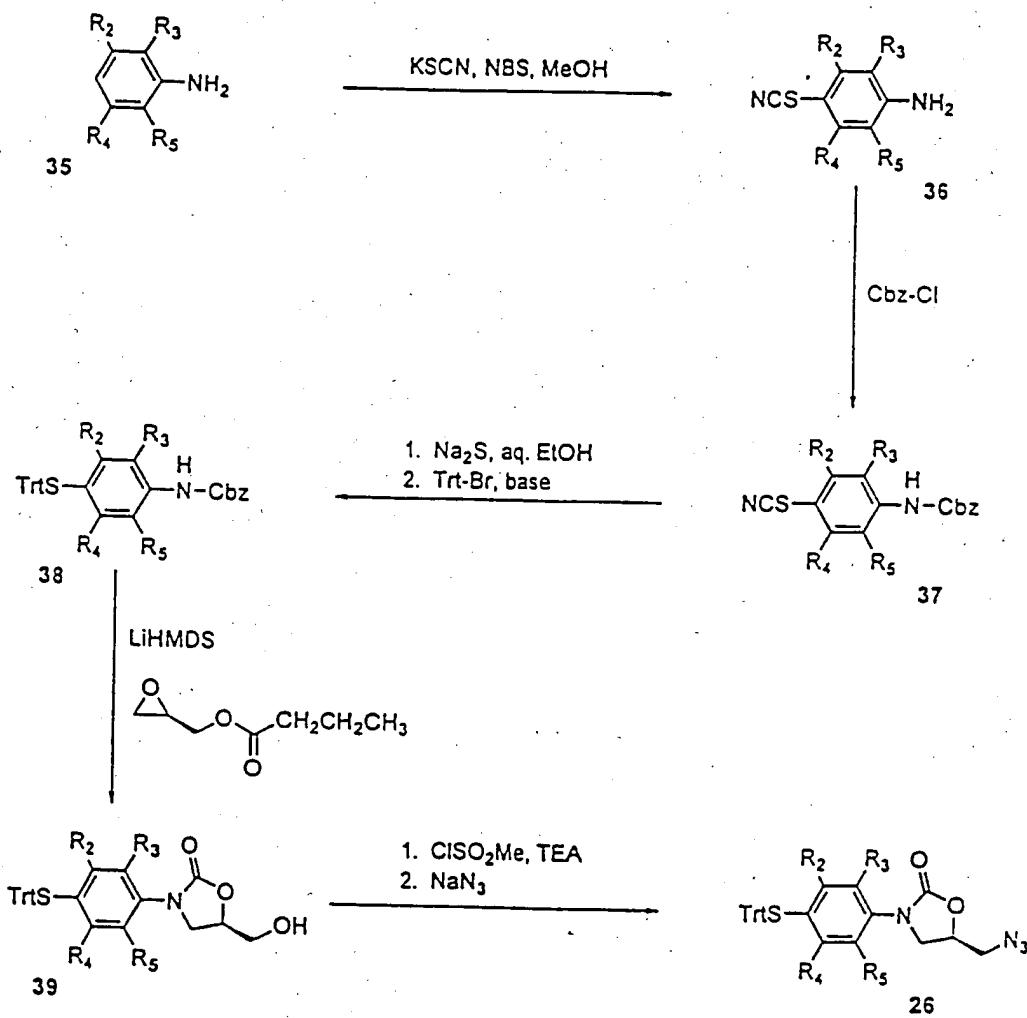


FIGURE 8

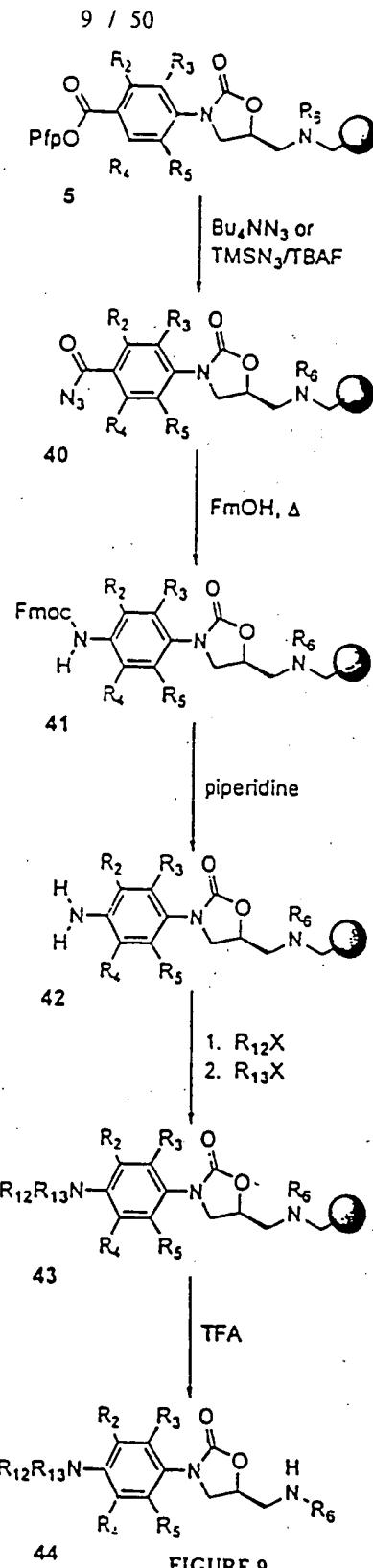


FIGURE 9

10 / 50

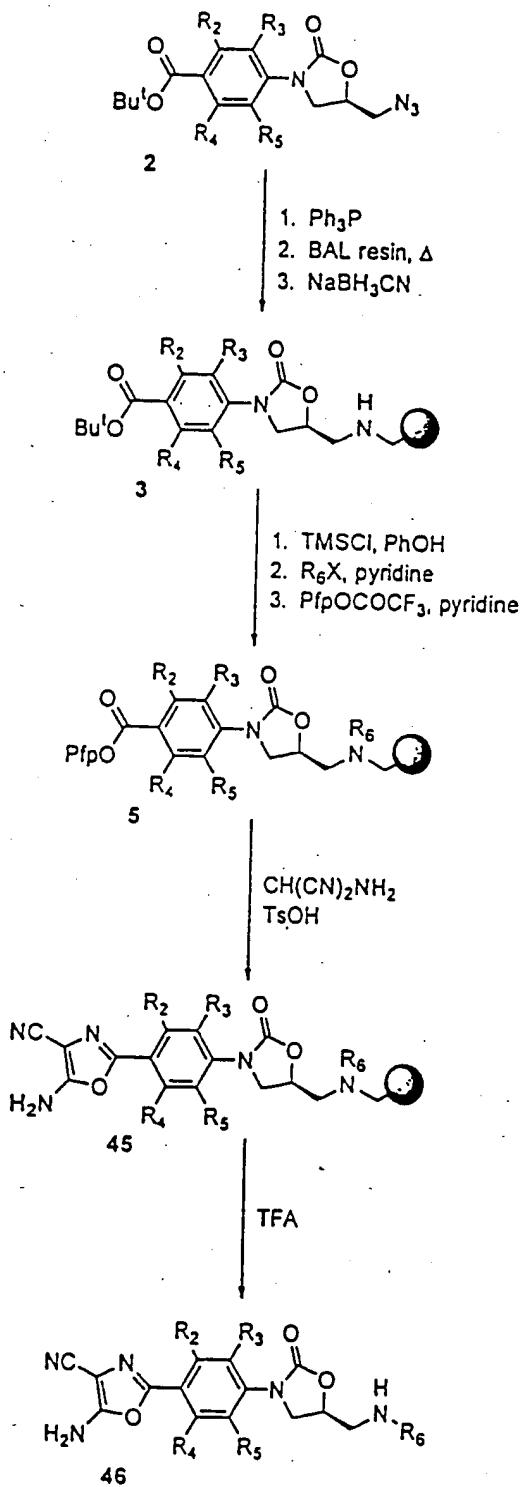


FIGURE 10

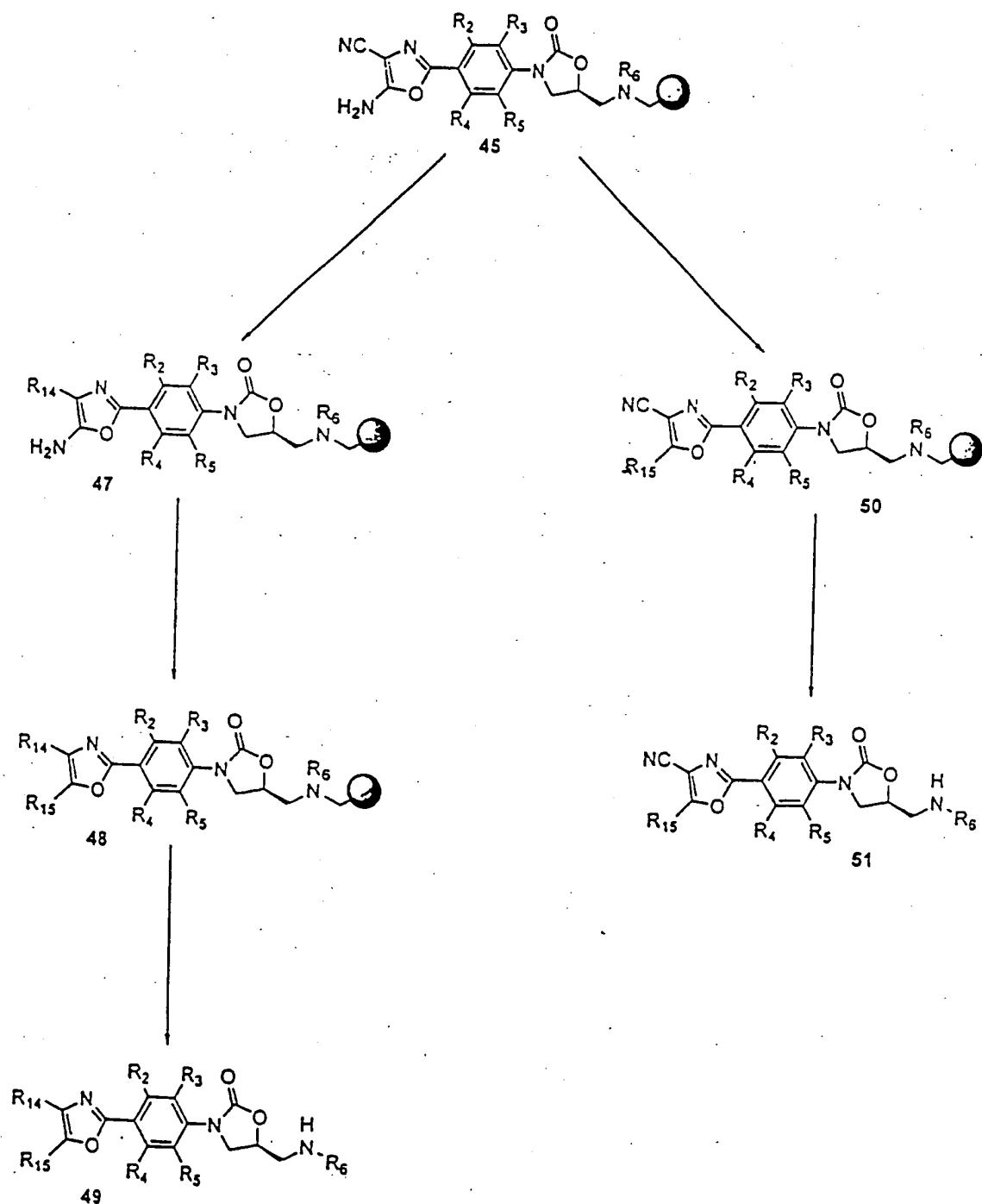


FIGURE 11

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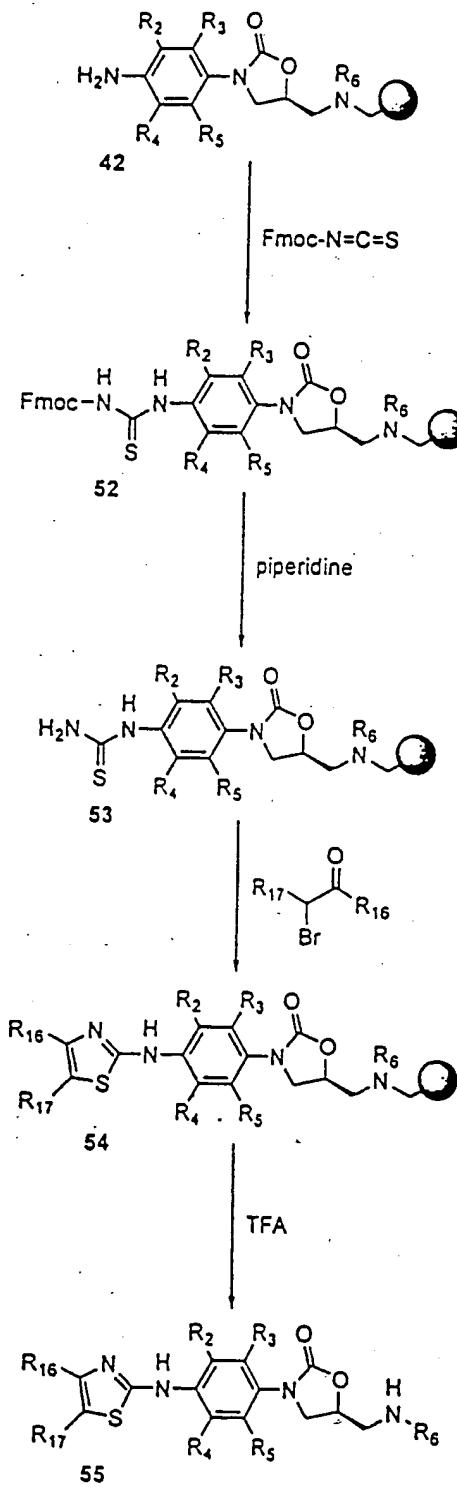


FIGURE 12

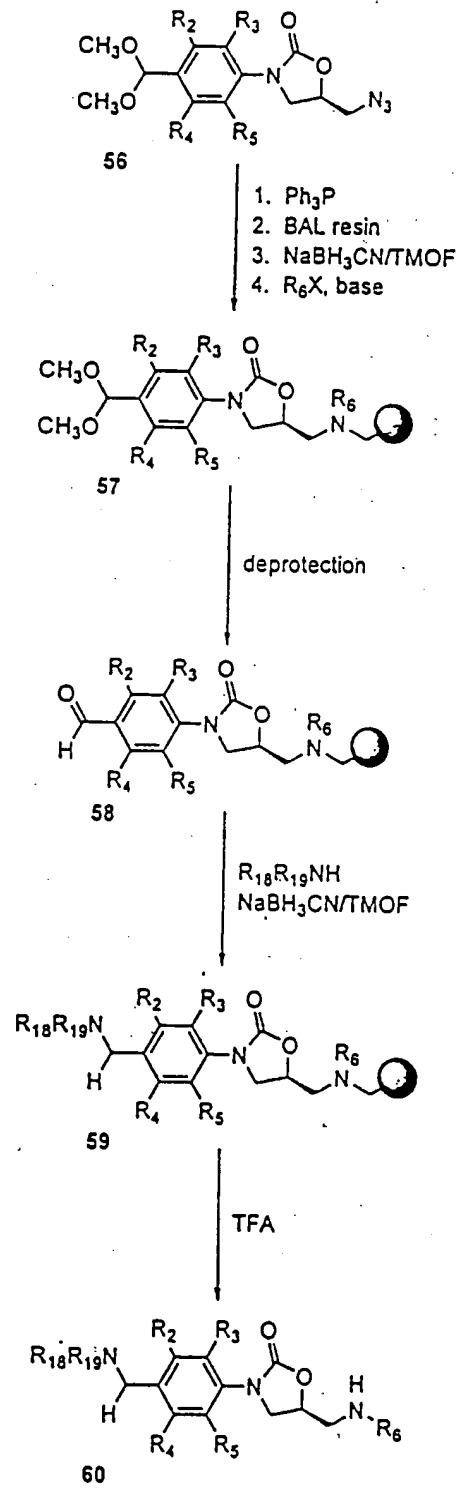


FIGURE 13

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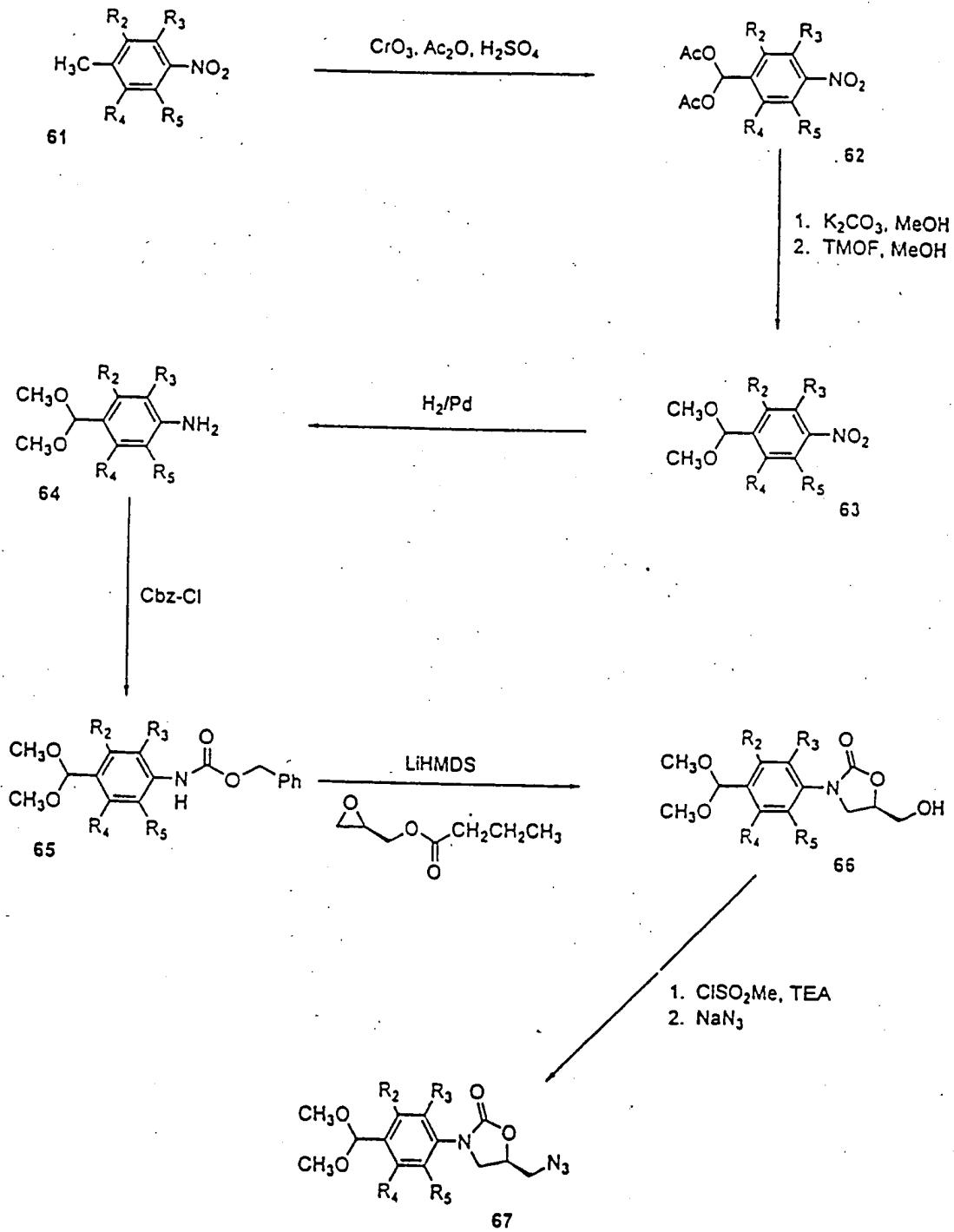


FIGURE 14

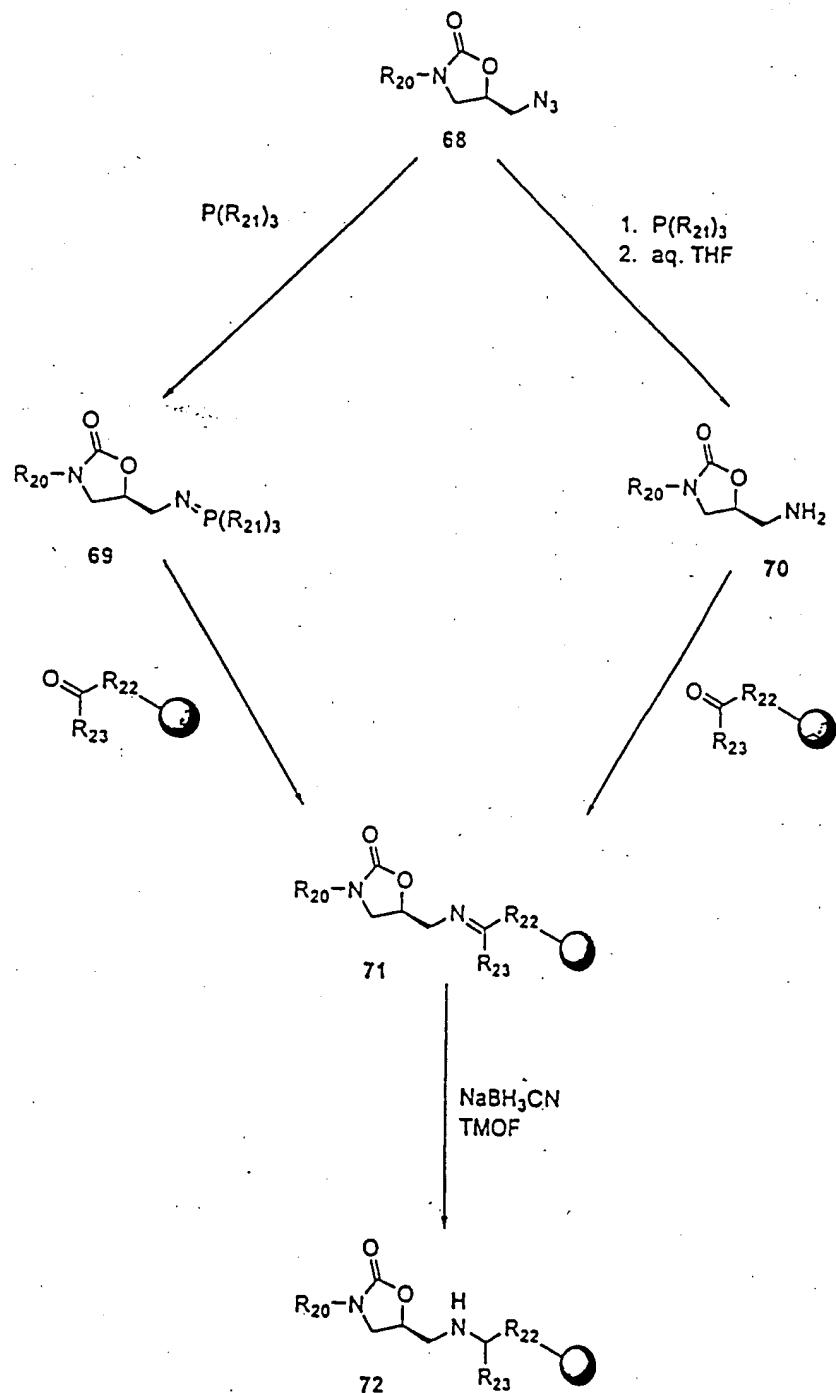


FIGURE 15

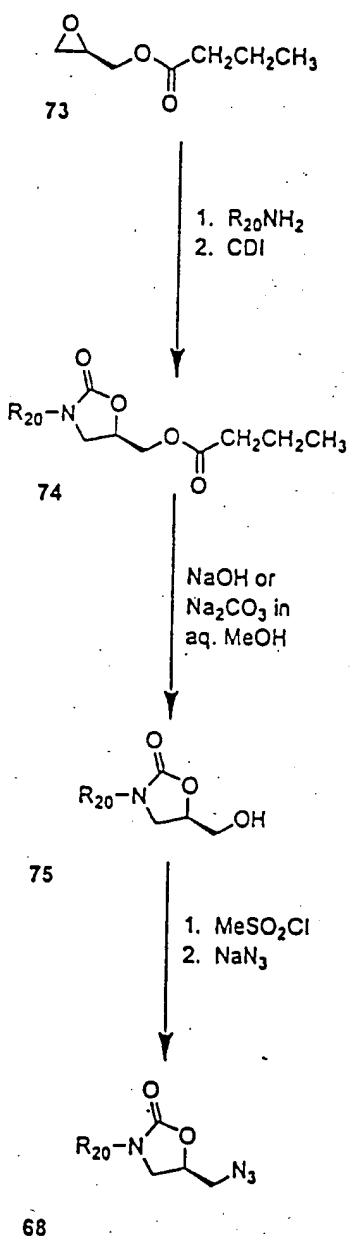
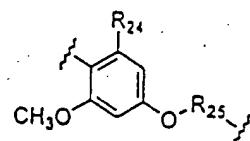


FIGURE 16



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FIGURE 17

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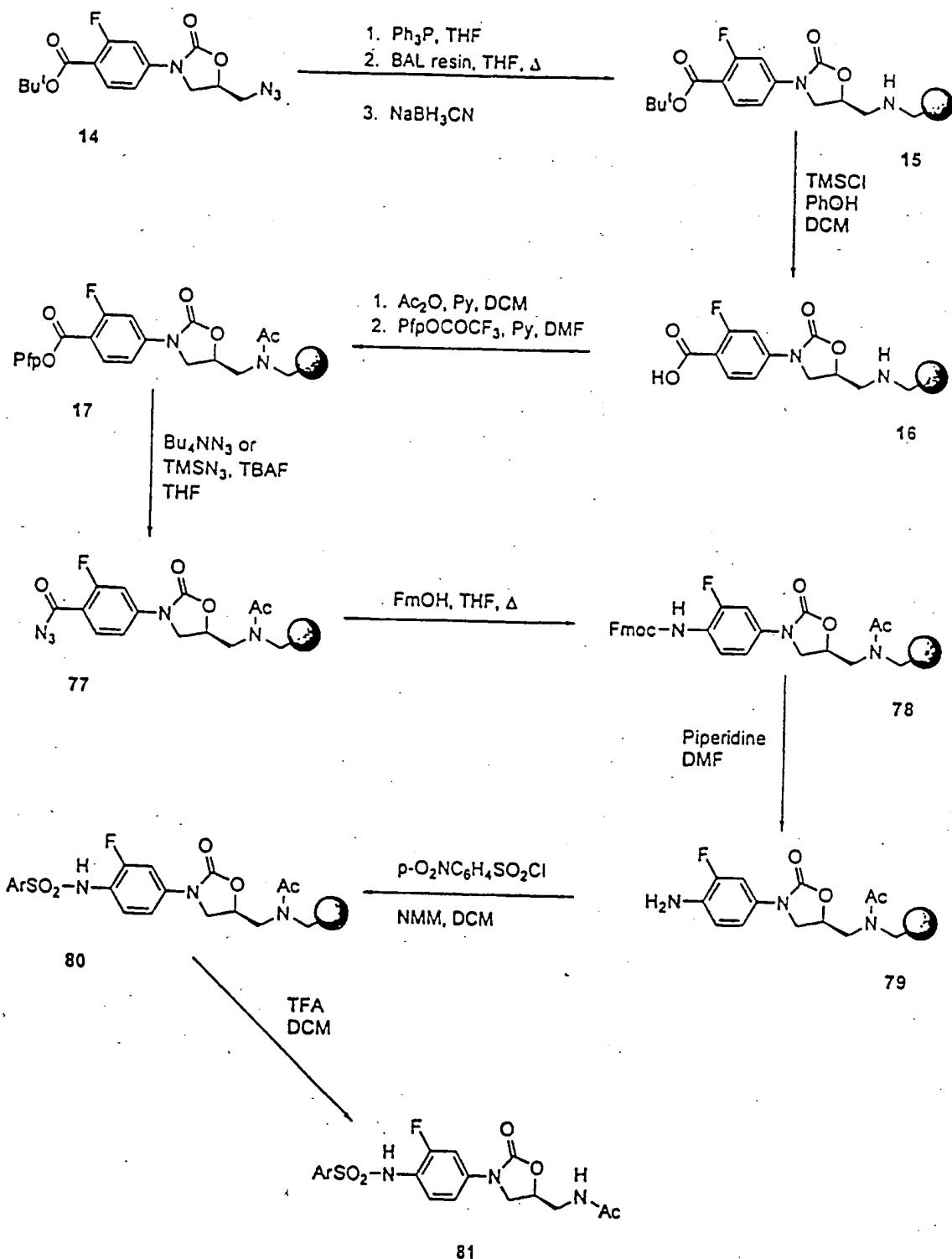


FIGURE 18

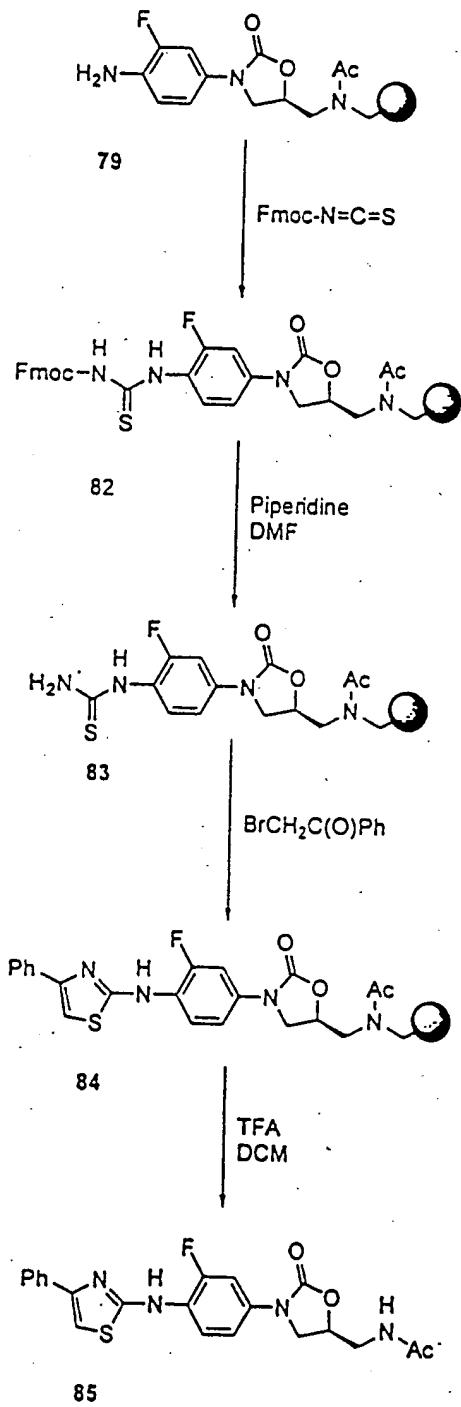


FIGURE 19

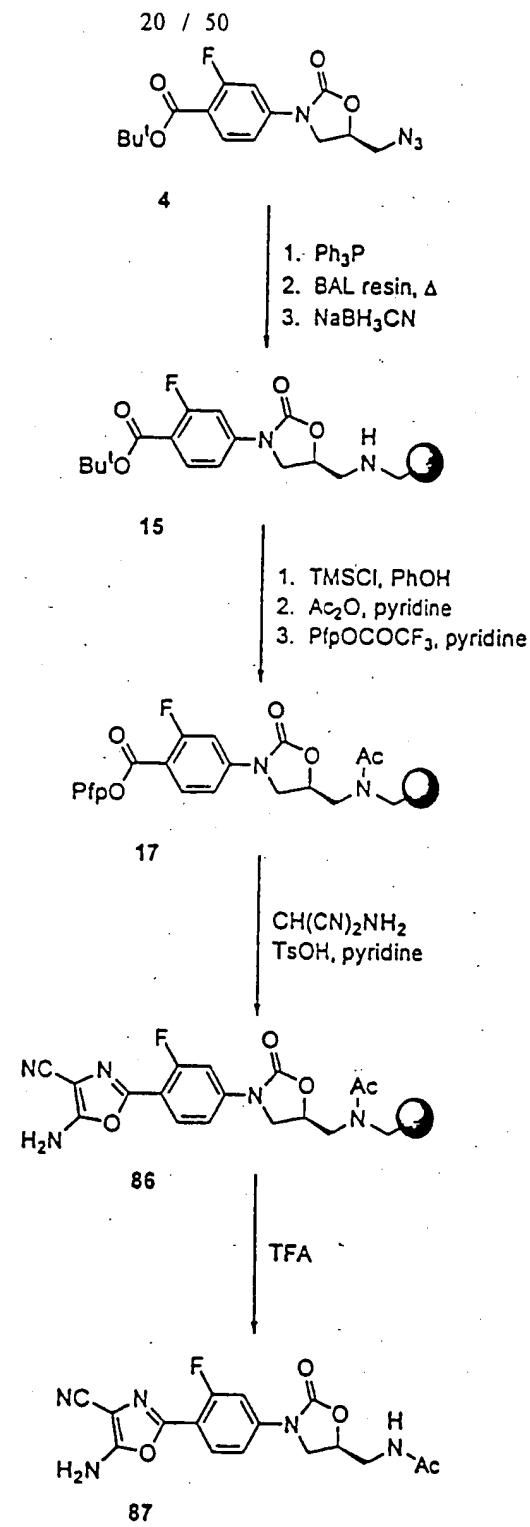


FIGURE 20

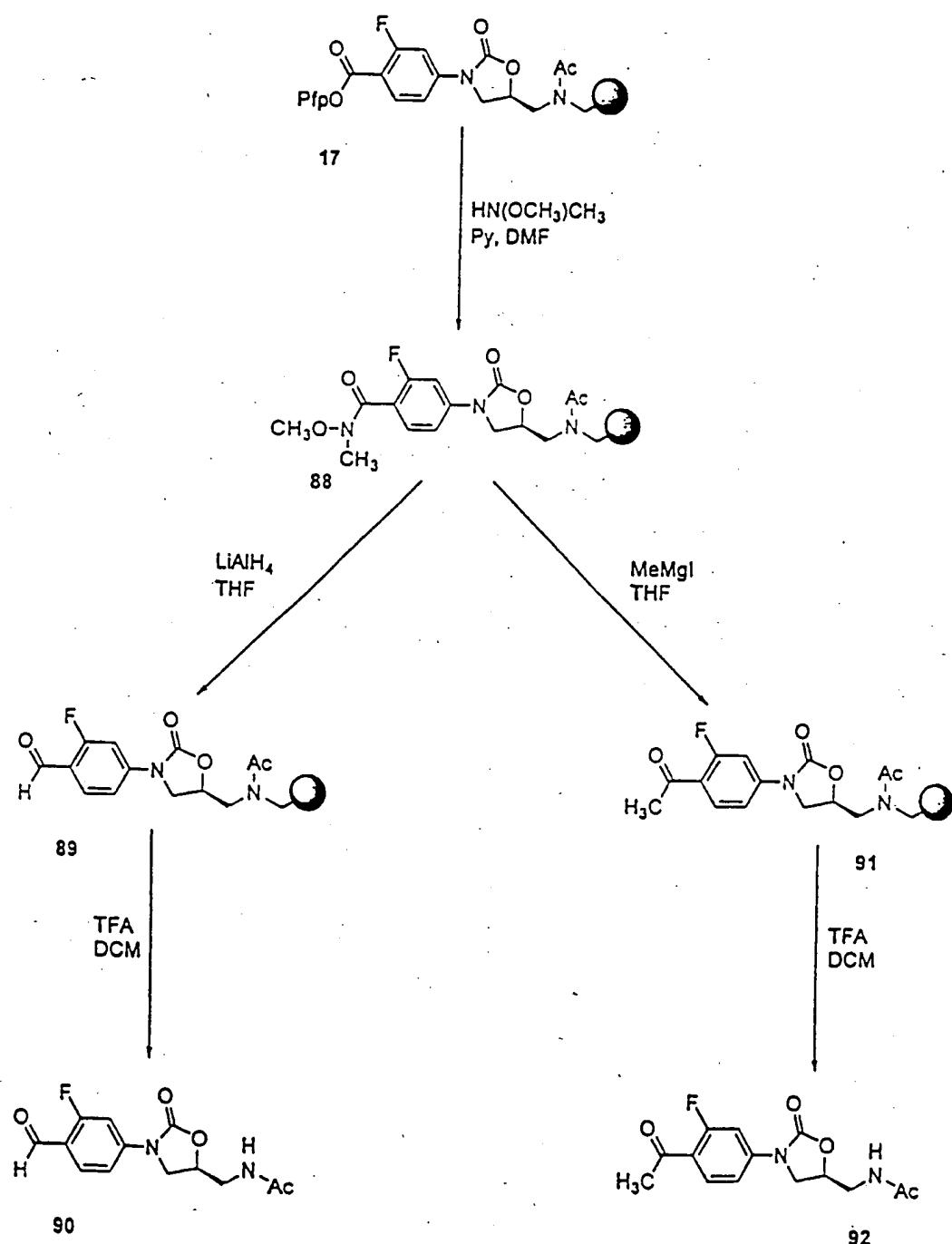


FIGURE 21

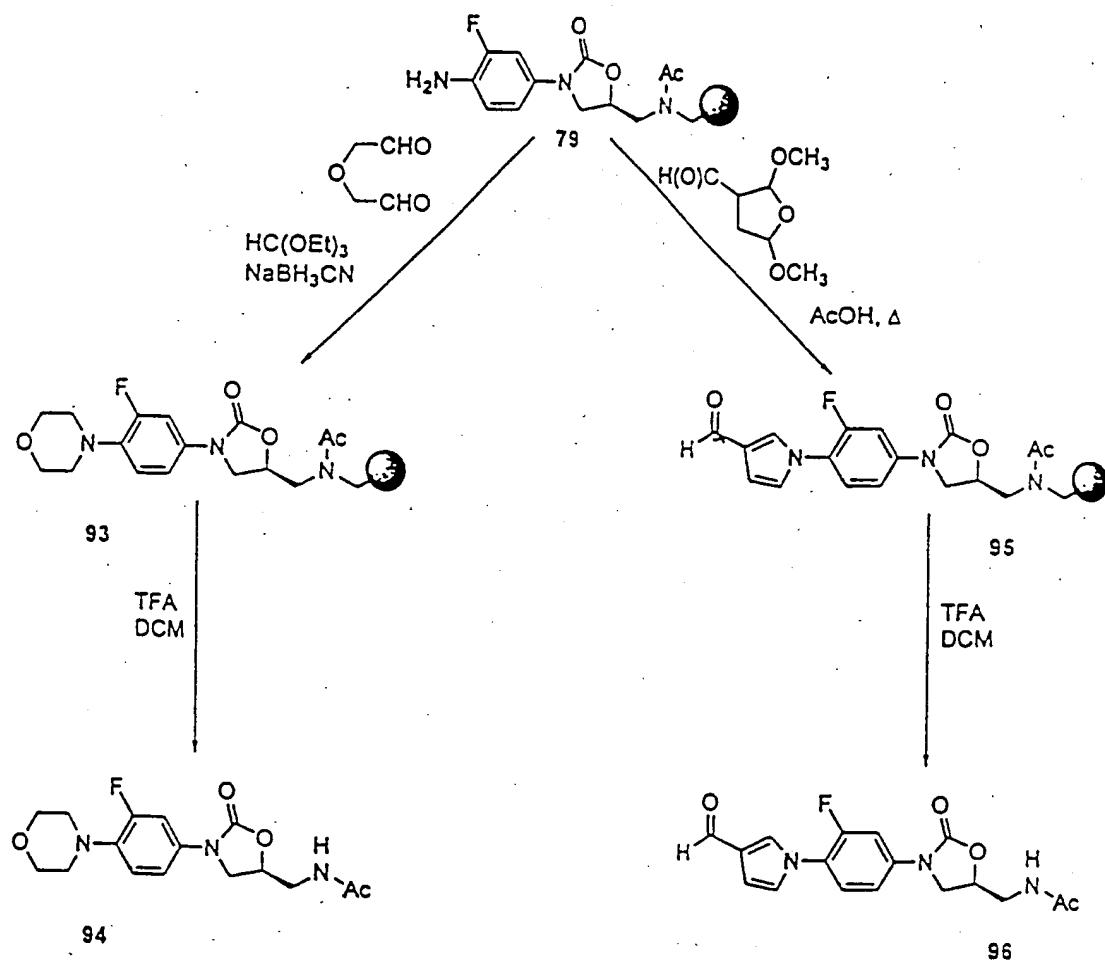


FIGURE 22

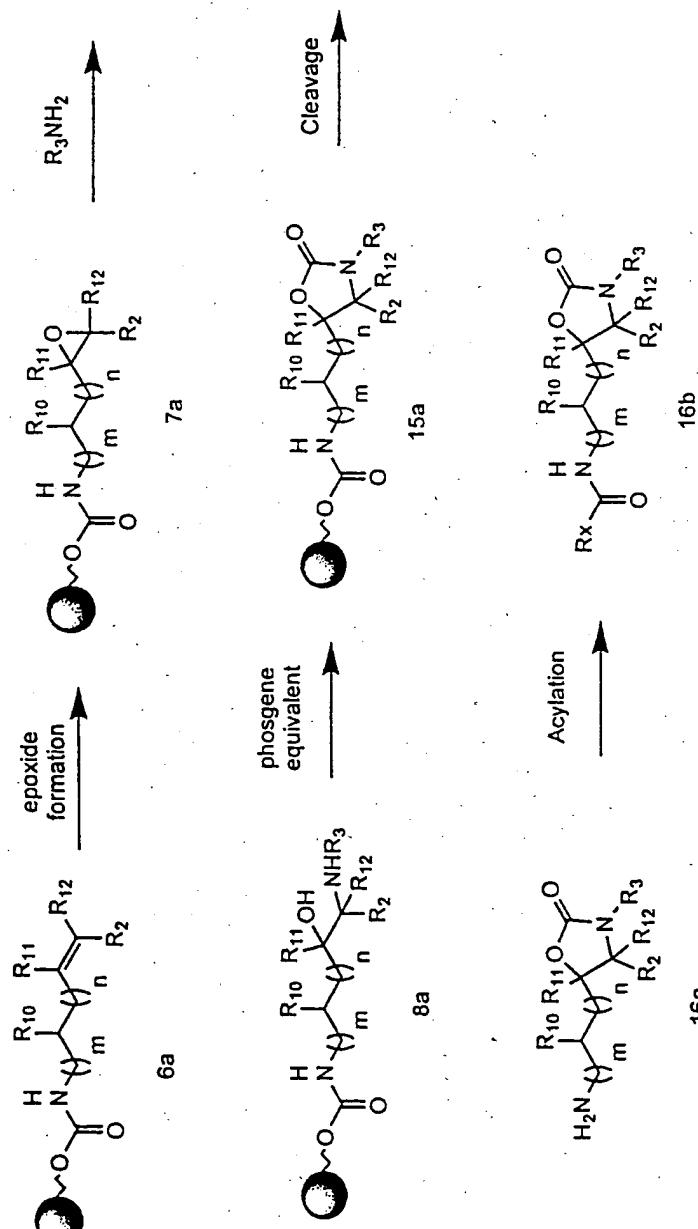


FIGURE 23

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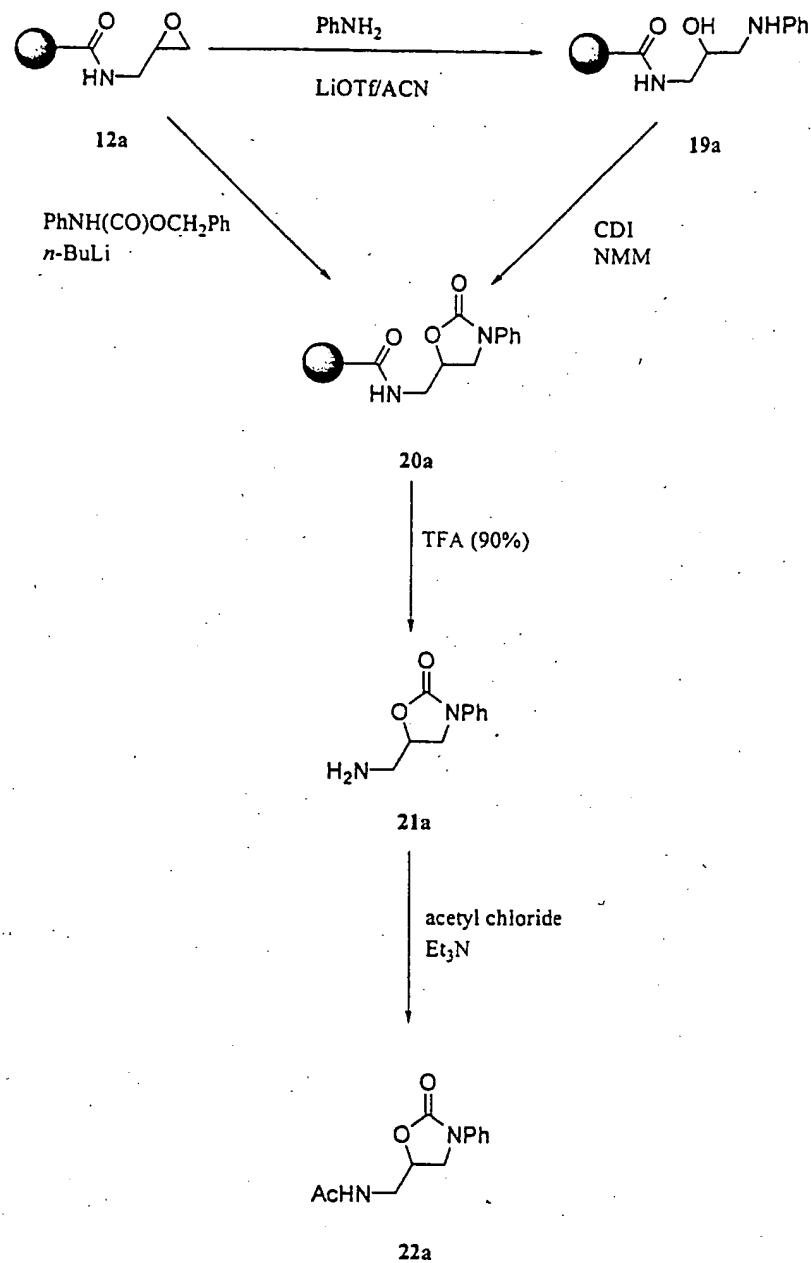


FIGURE 24

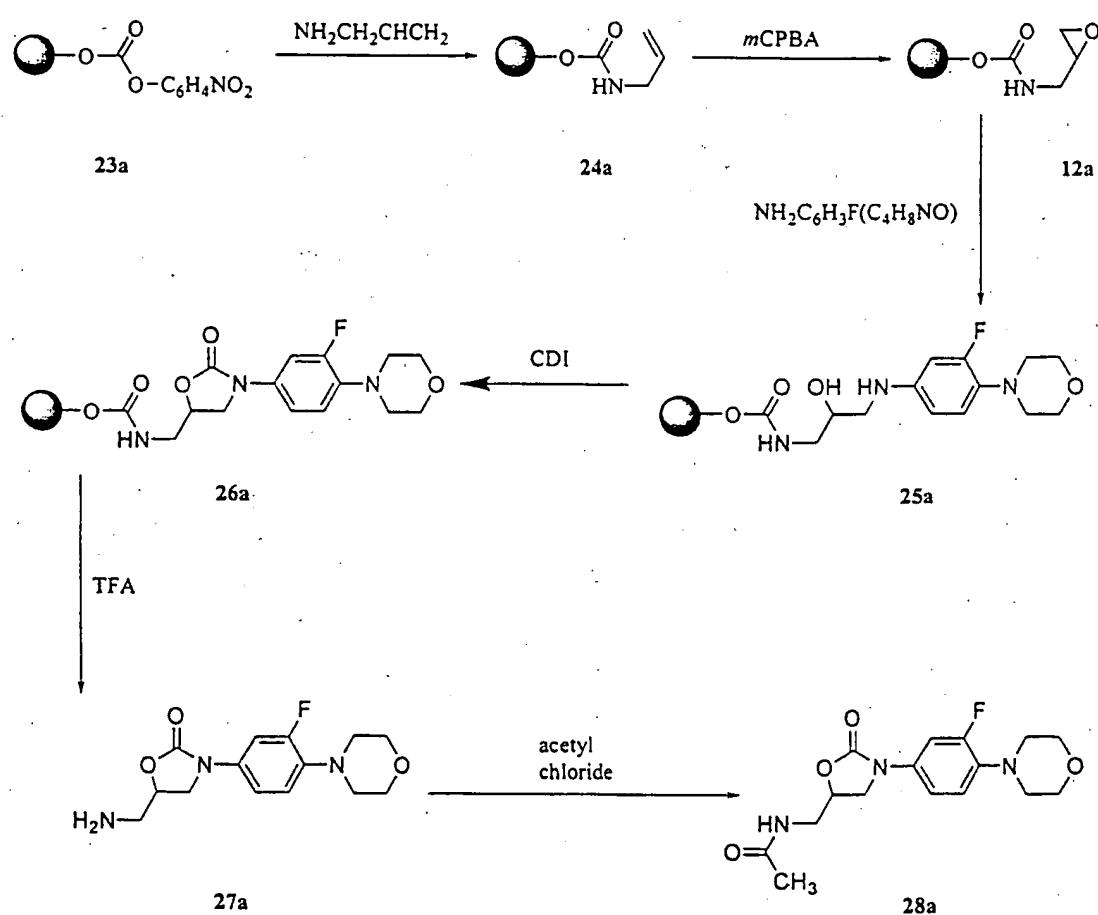


FIGURE 25

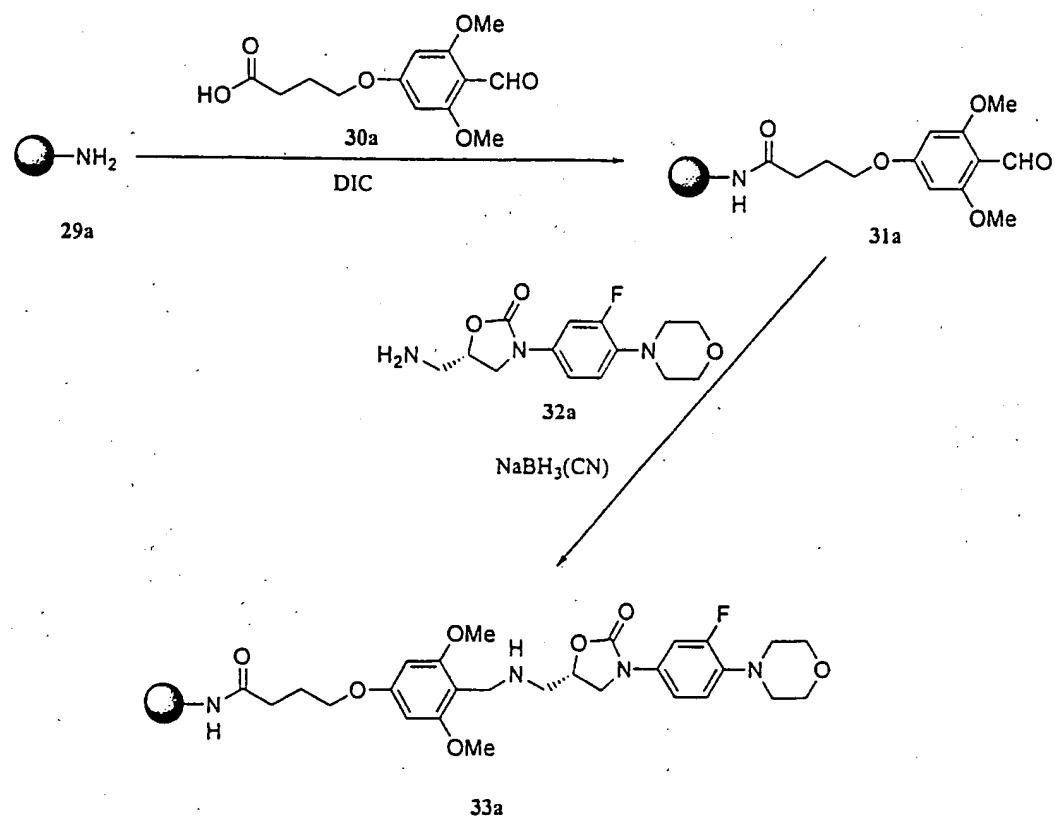


FIGURE 26

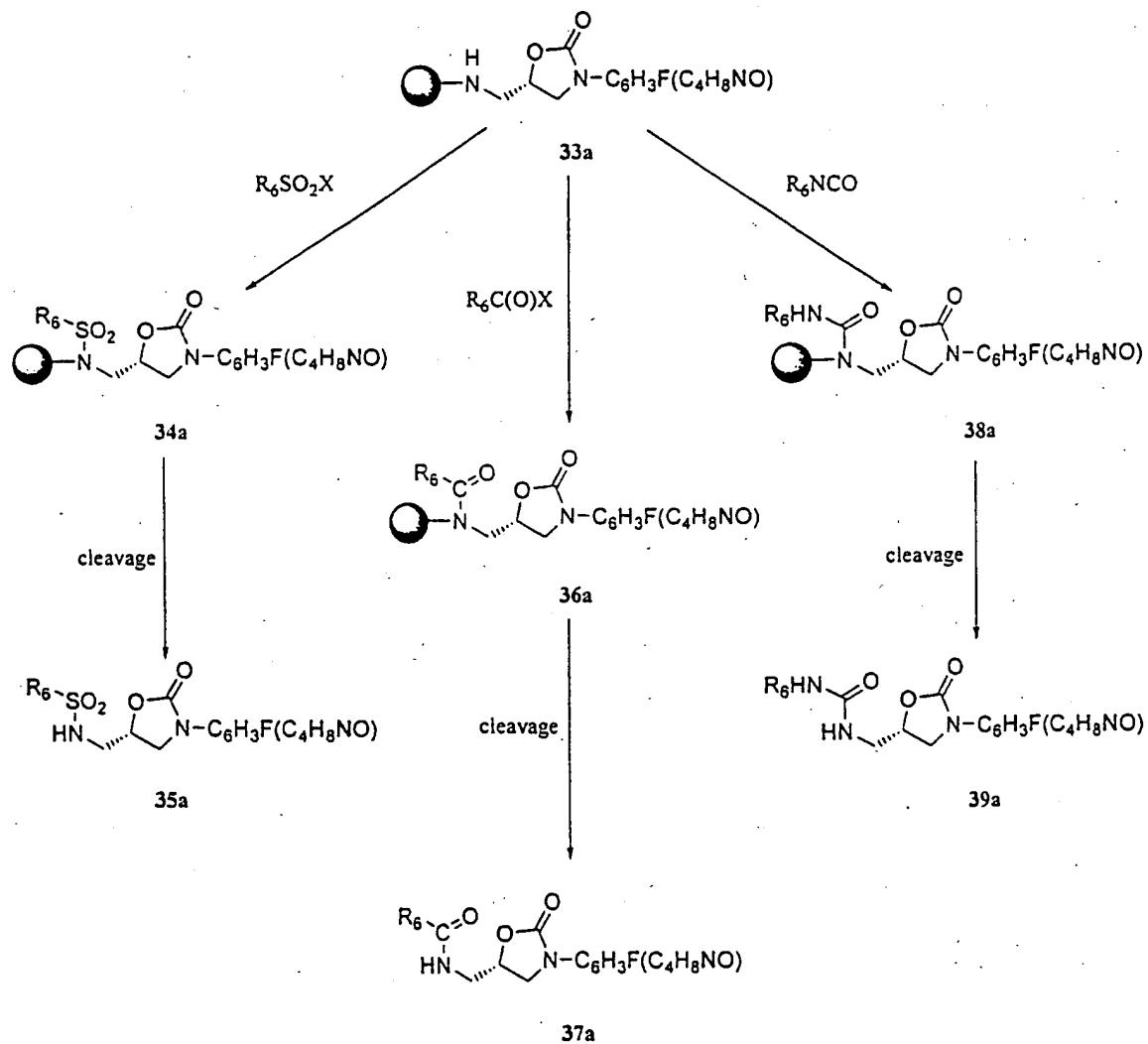


FIGURE 27

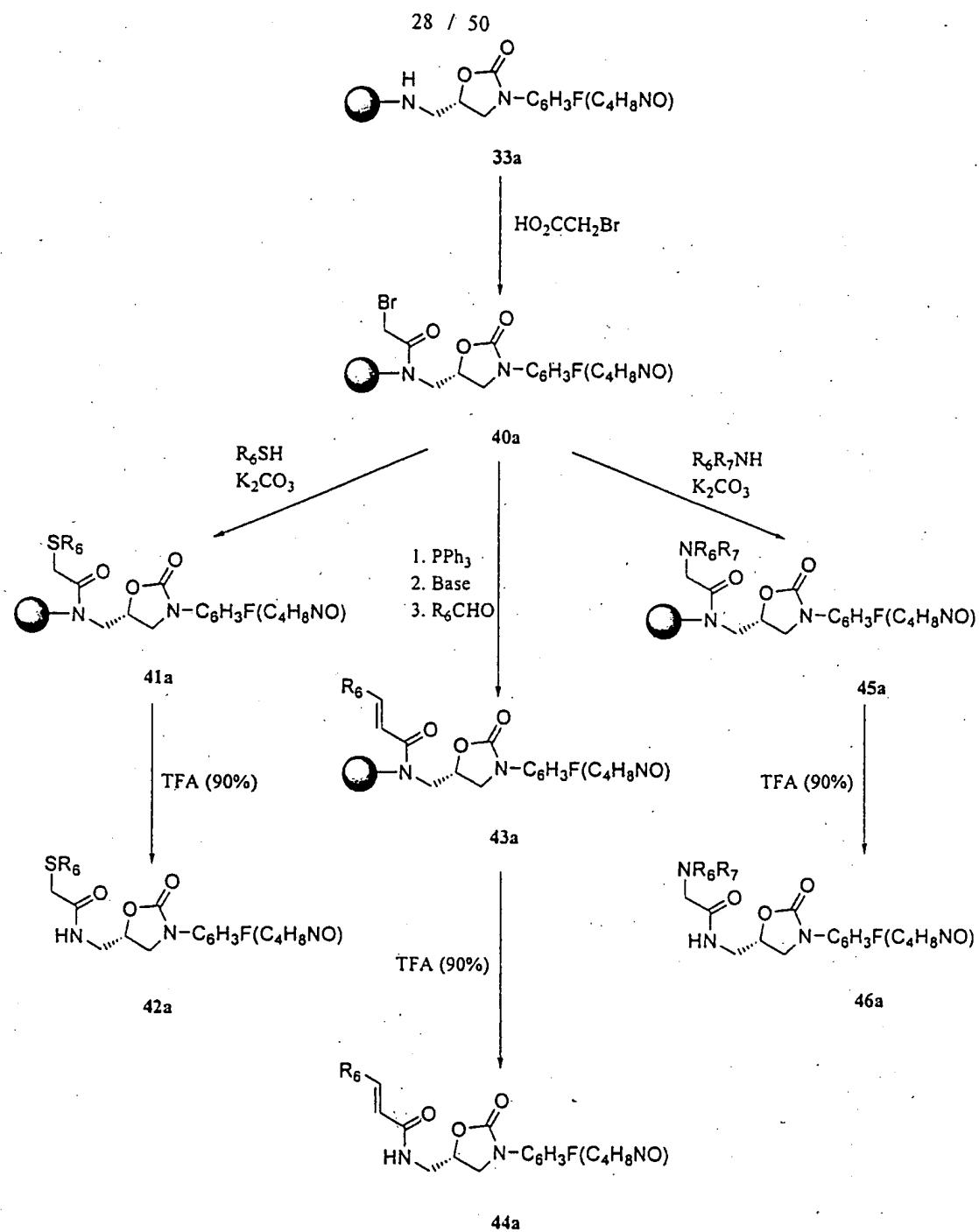


FIGURE 28

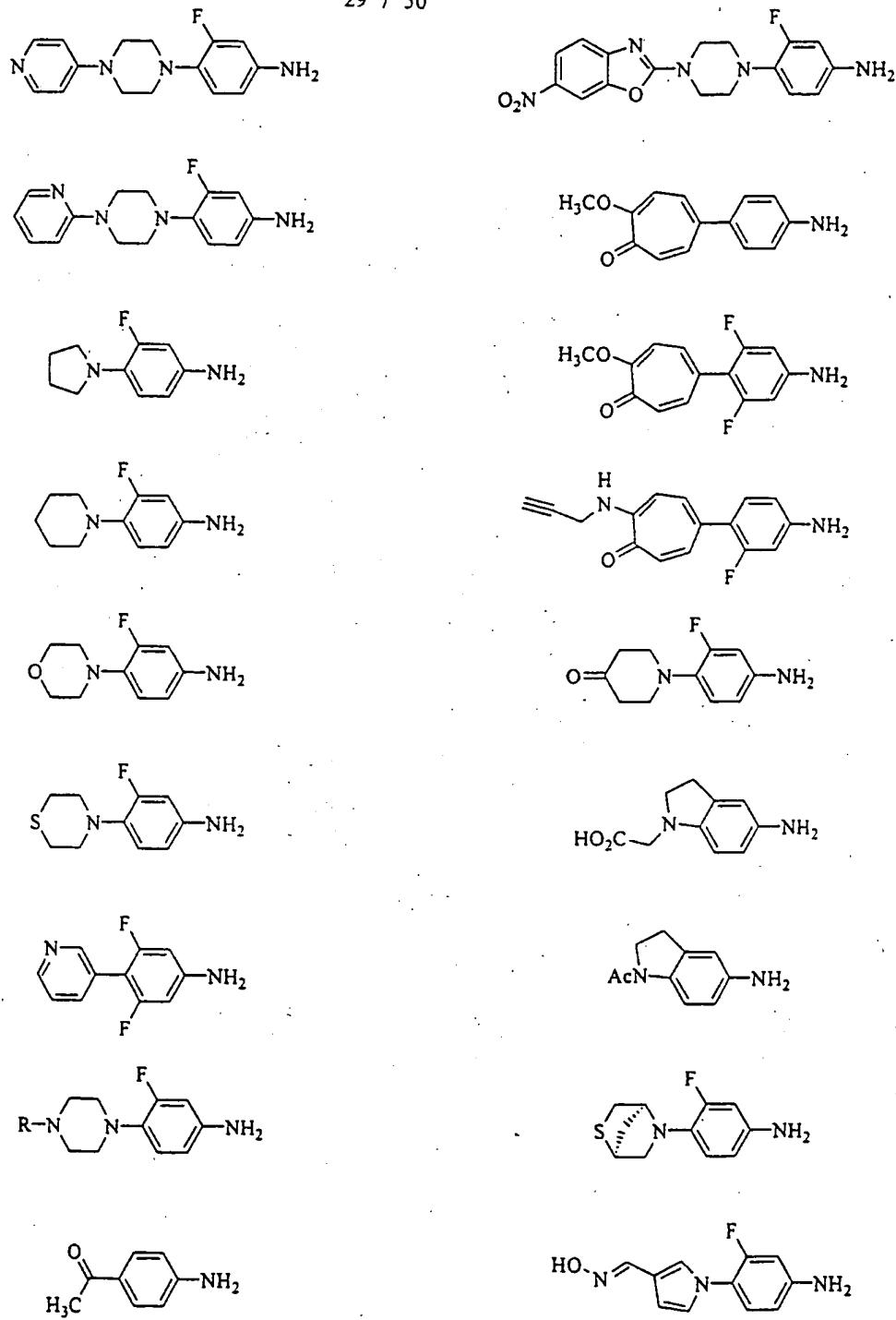


FIGURE 29

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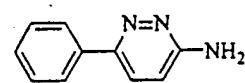
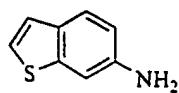
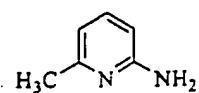
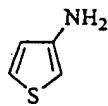
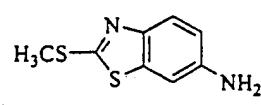
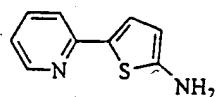
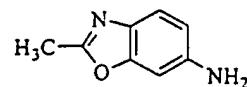
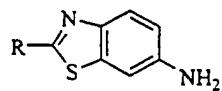
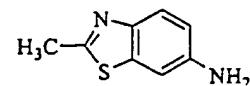
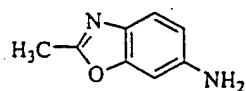
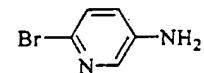
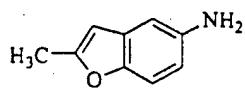
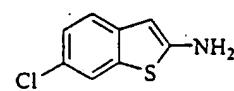
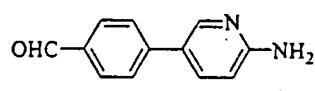
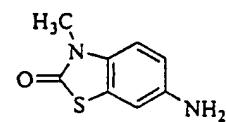
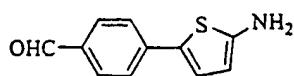
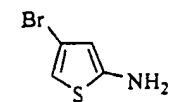
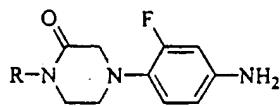
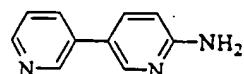


FIGURE 30

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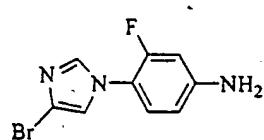
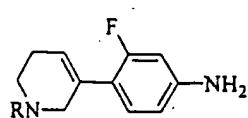
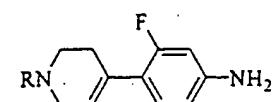
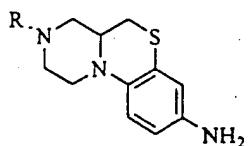
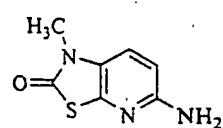
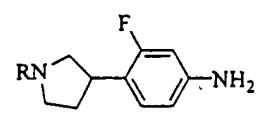
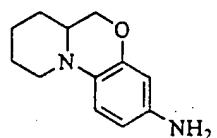
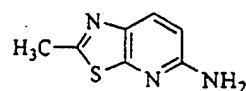
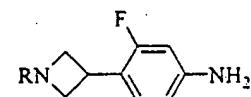
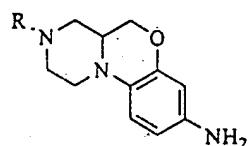
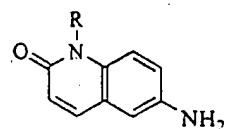
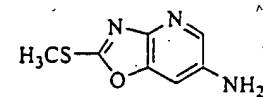
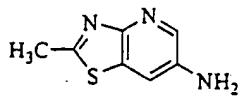
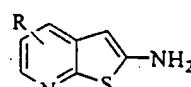
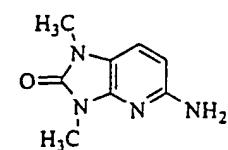
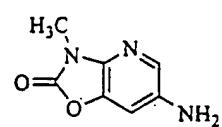


FIGURE 31

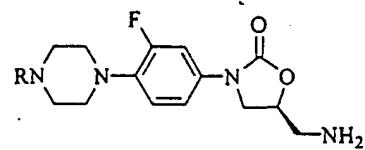
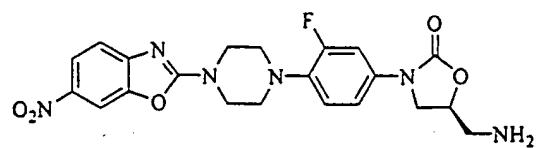
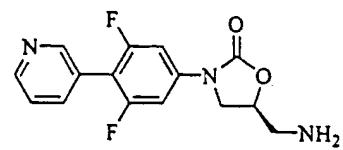
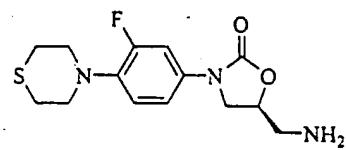
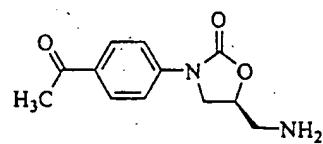
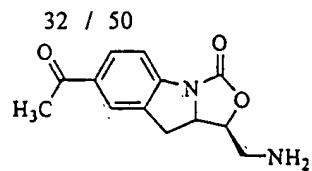


FIGURE 32

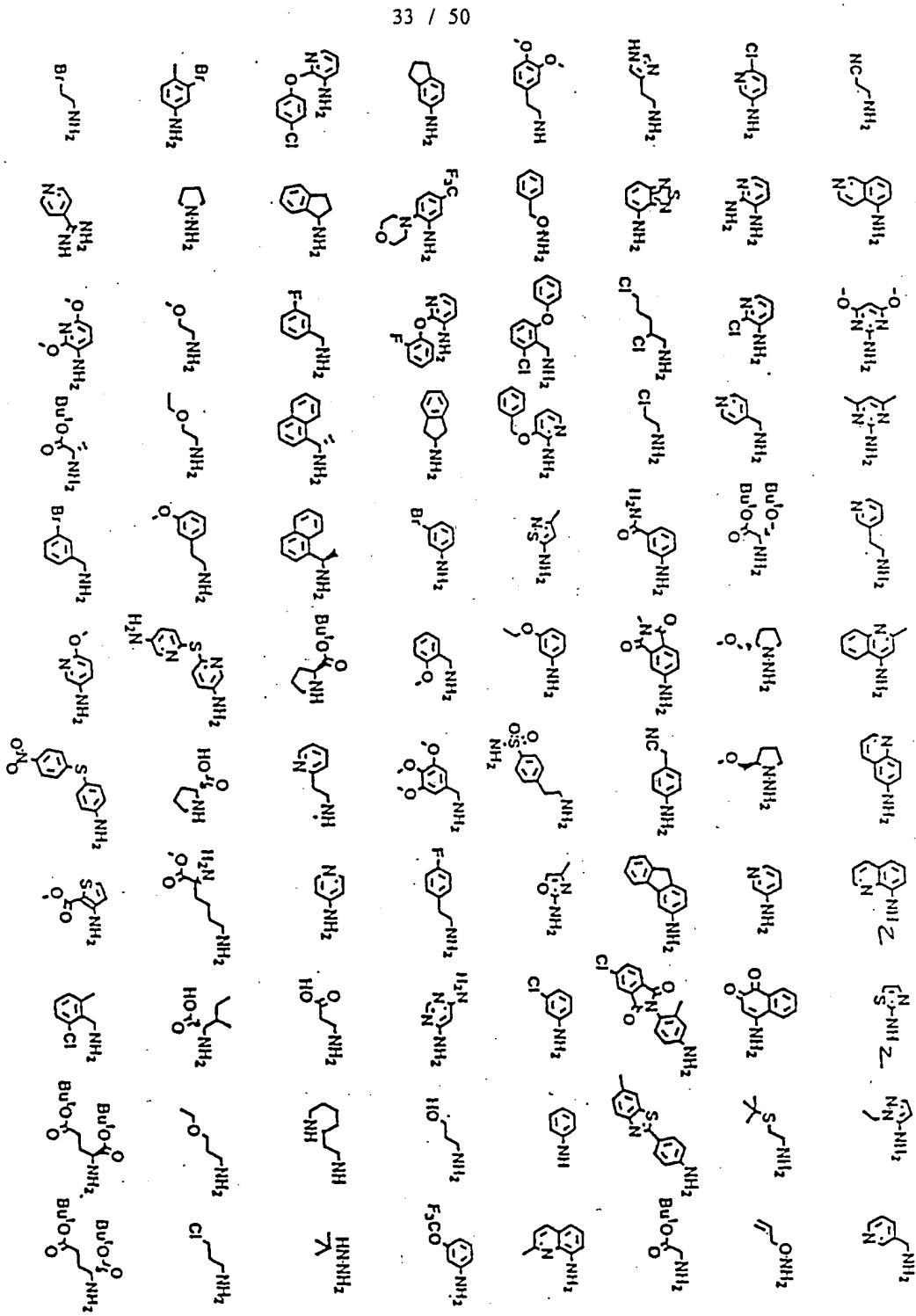


FIGURE 33

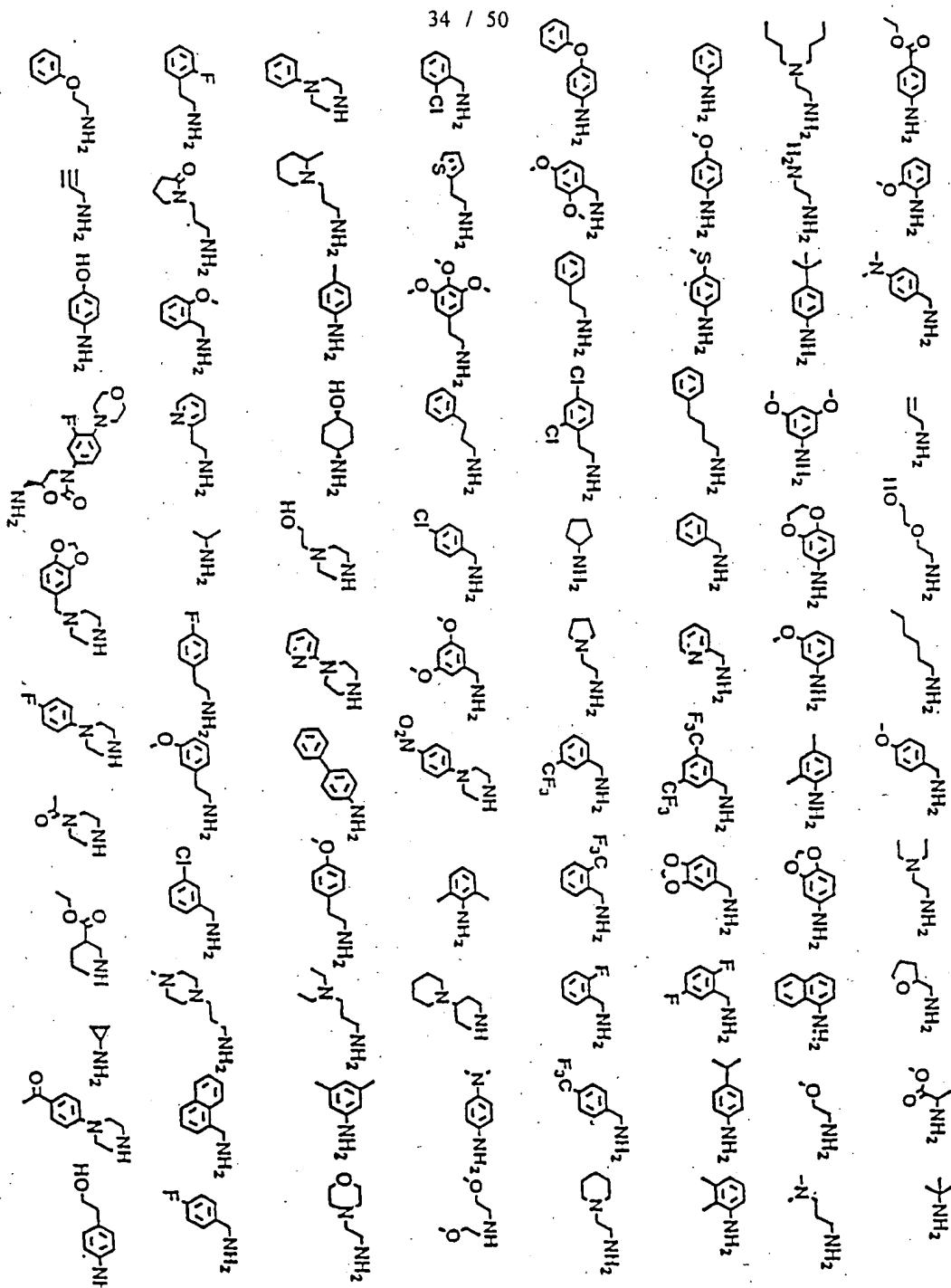


FIGURE 34

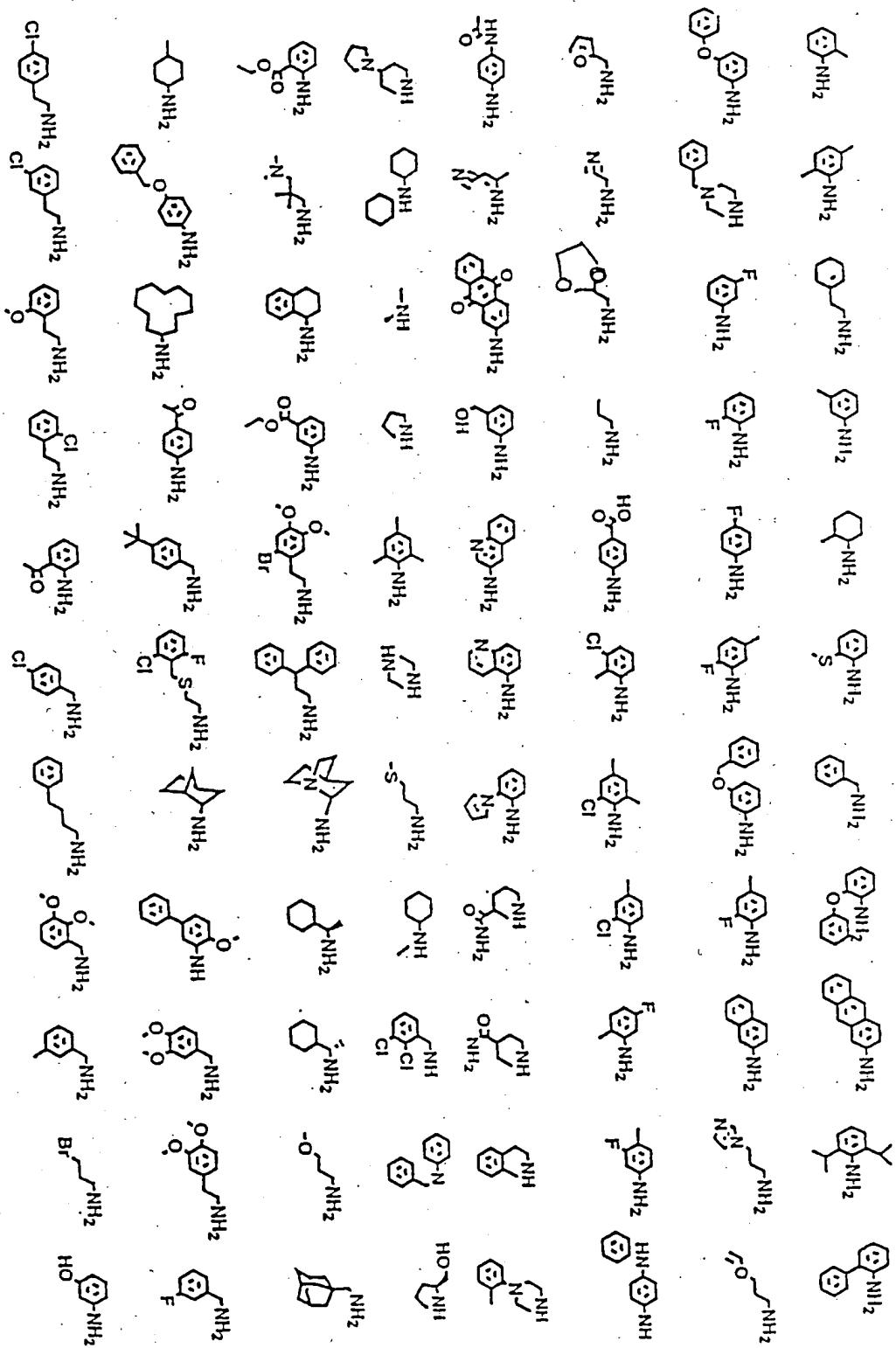


FIGURE 35

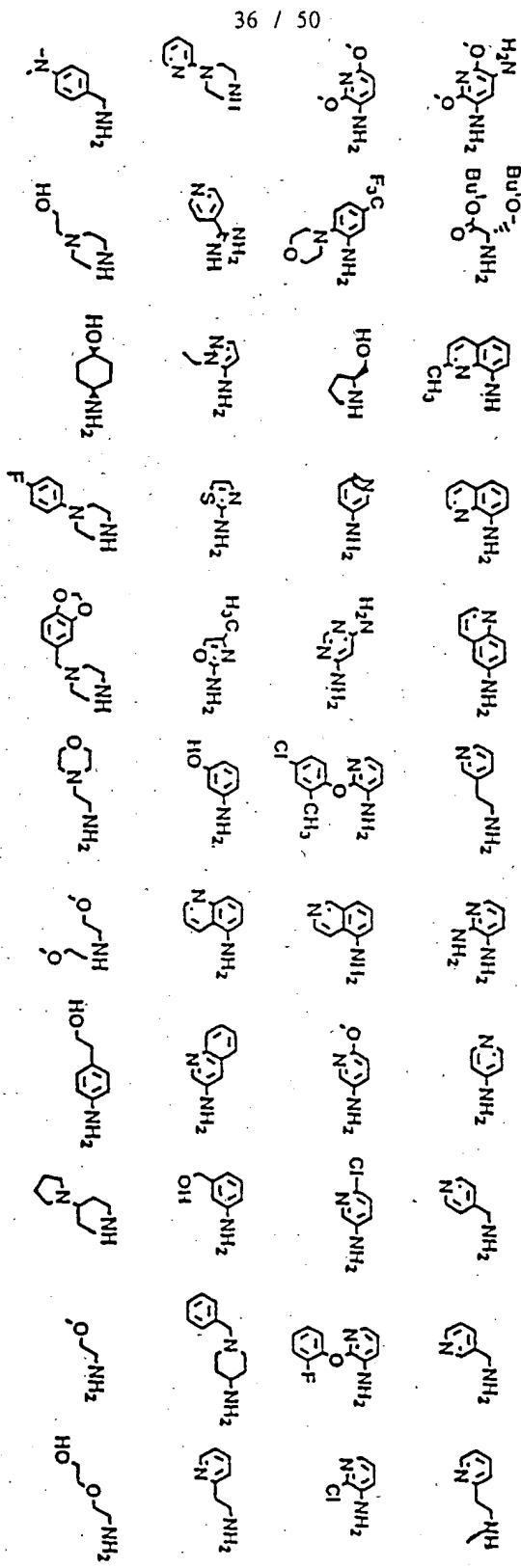


FIGURE 36

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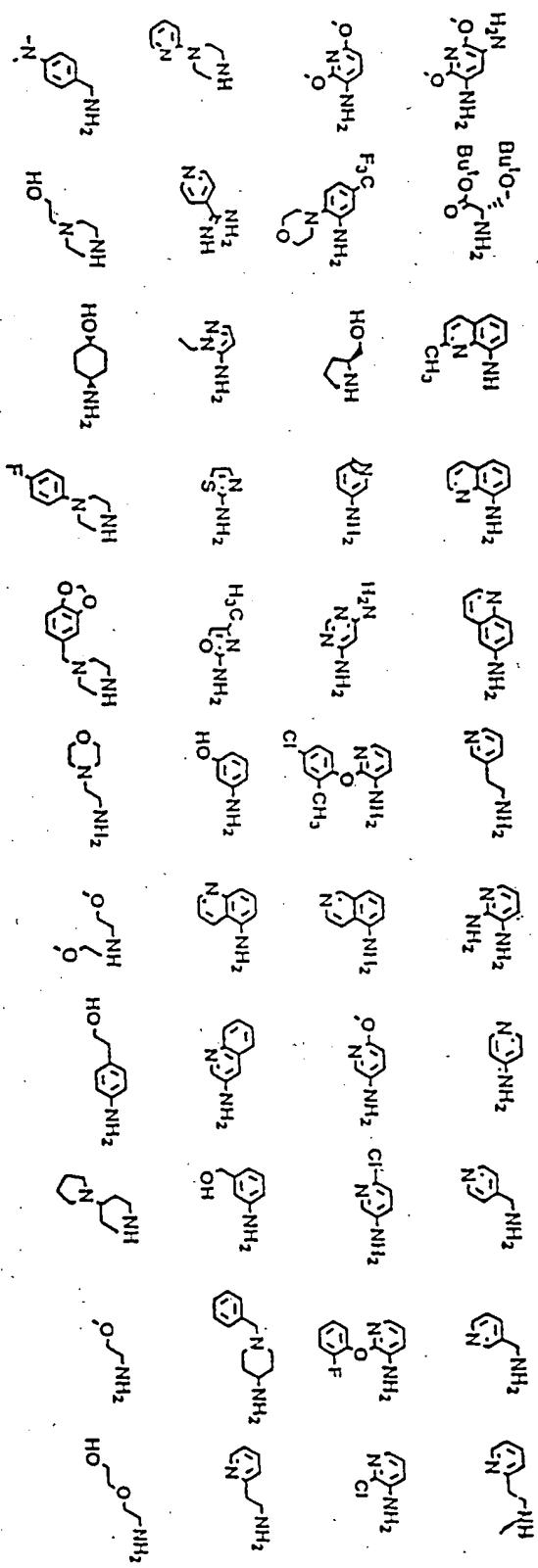


FIGURE 37

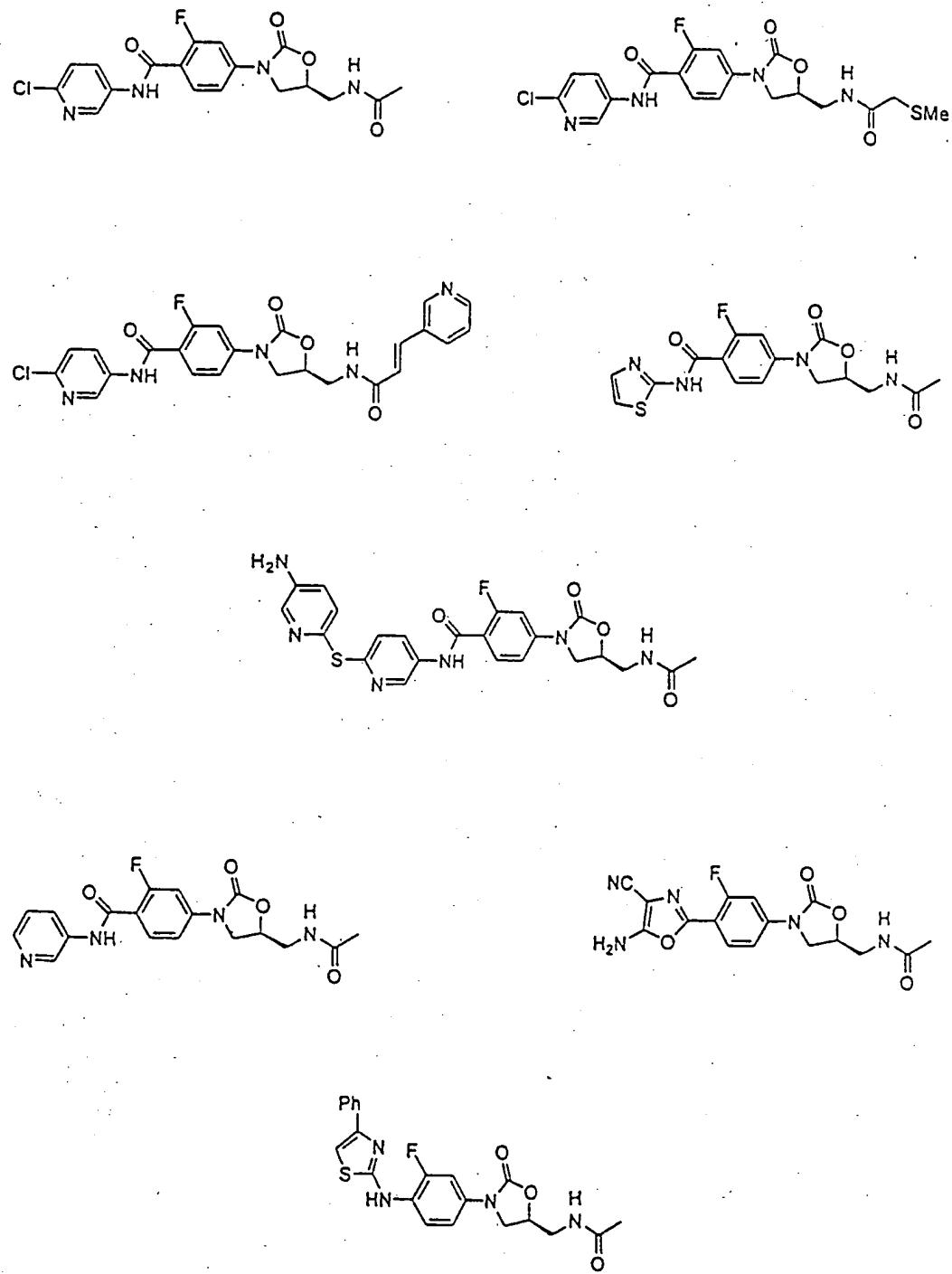


FIGURE 38

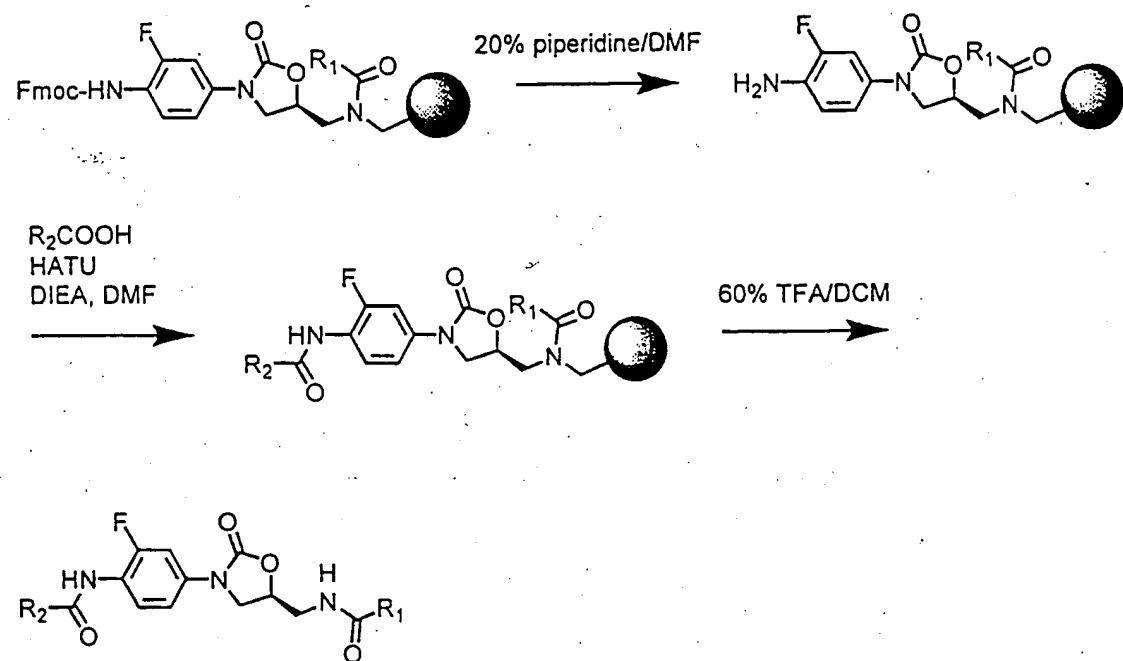


FIGURE 39

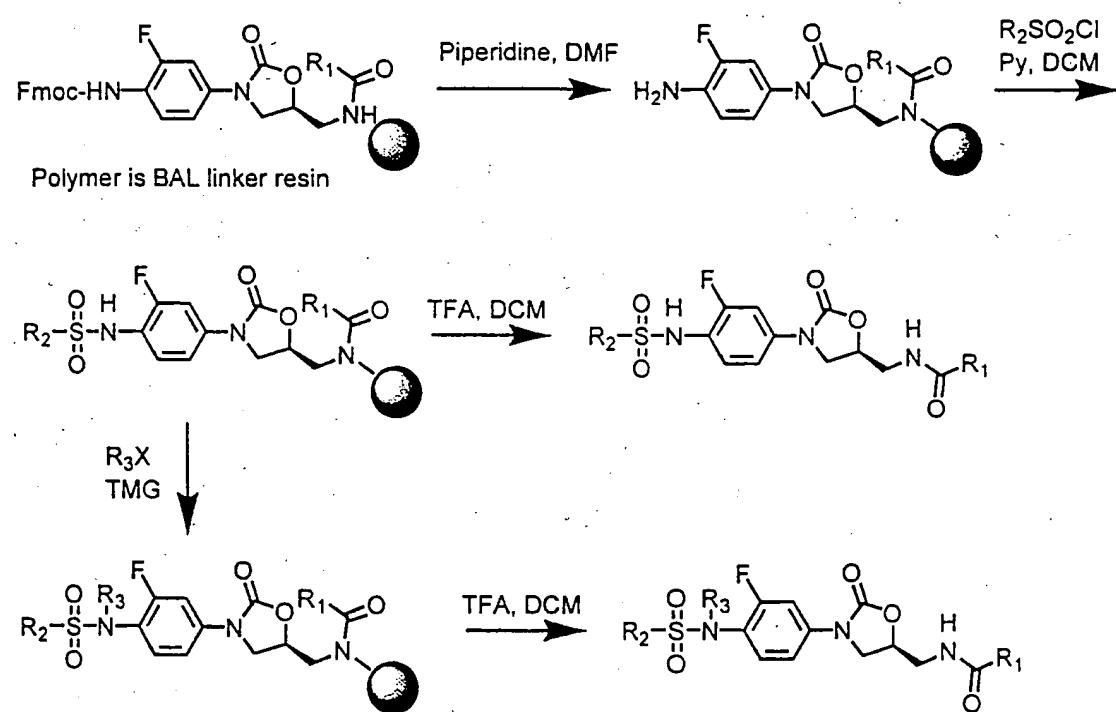


FIGURE 40

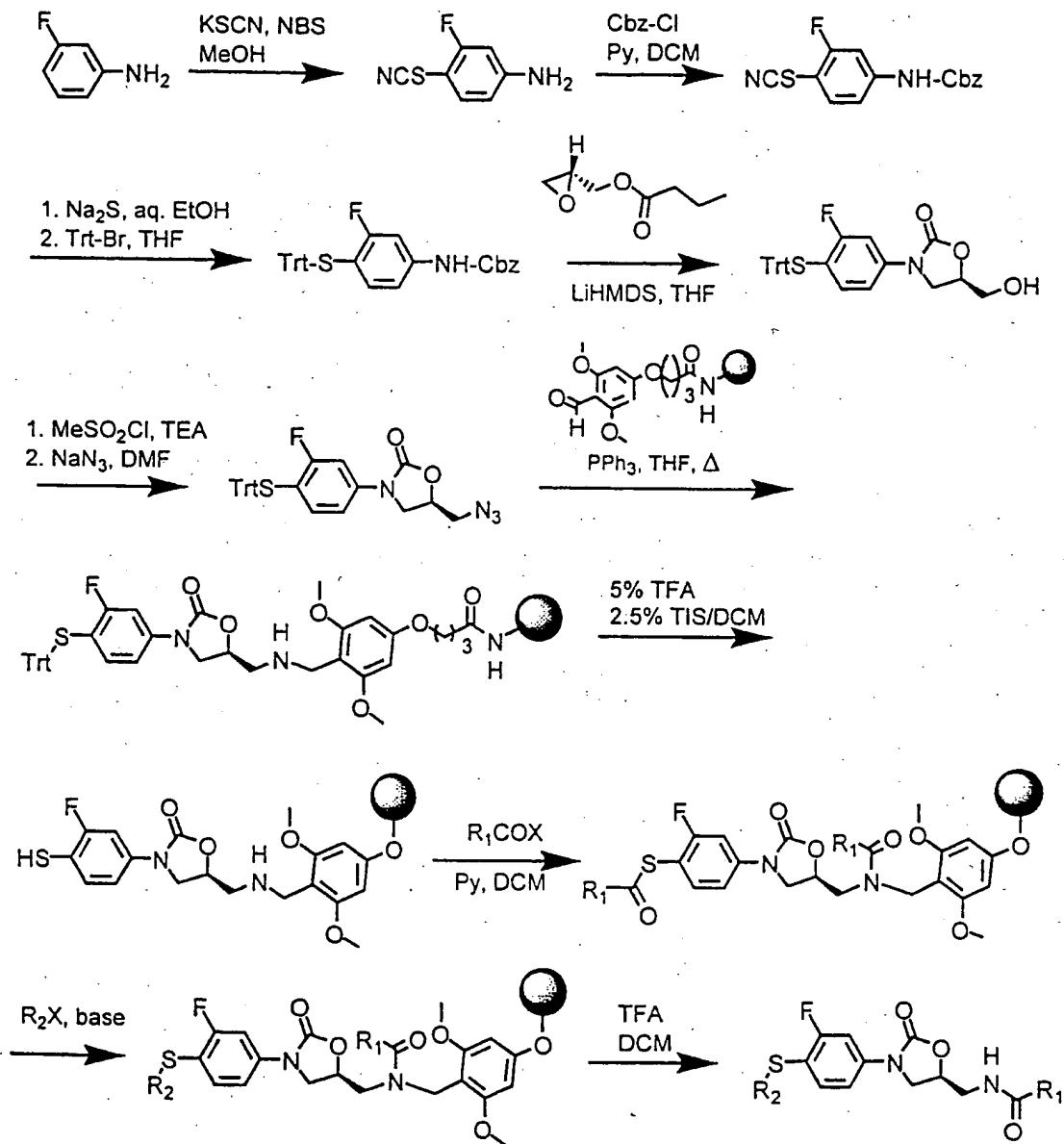


FIGURE 41

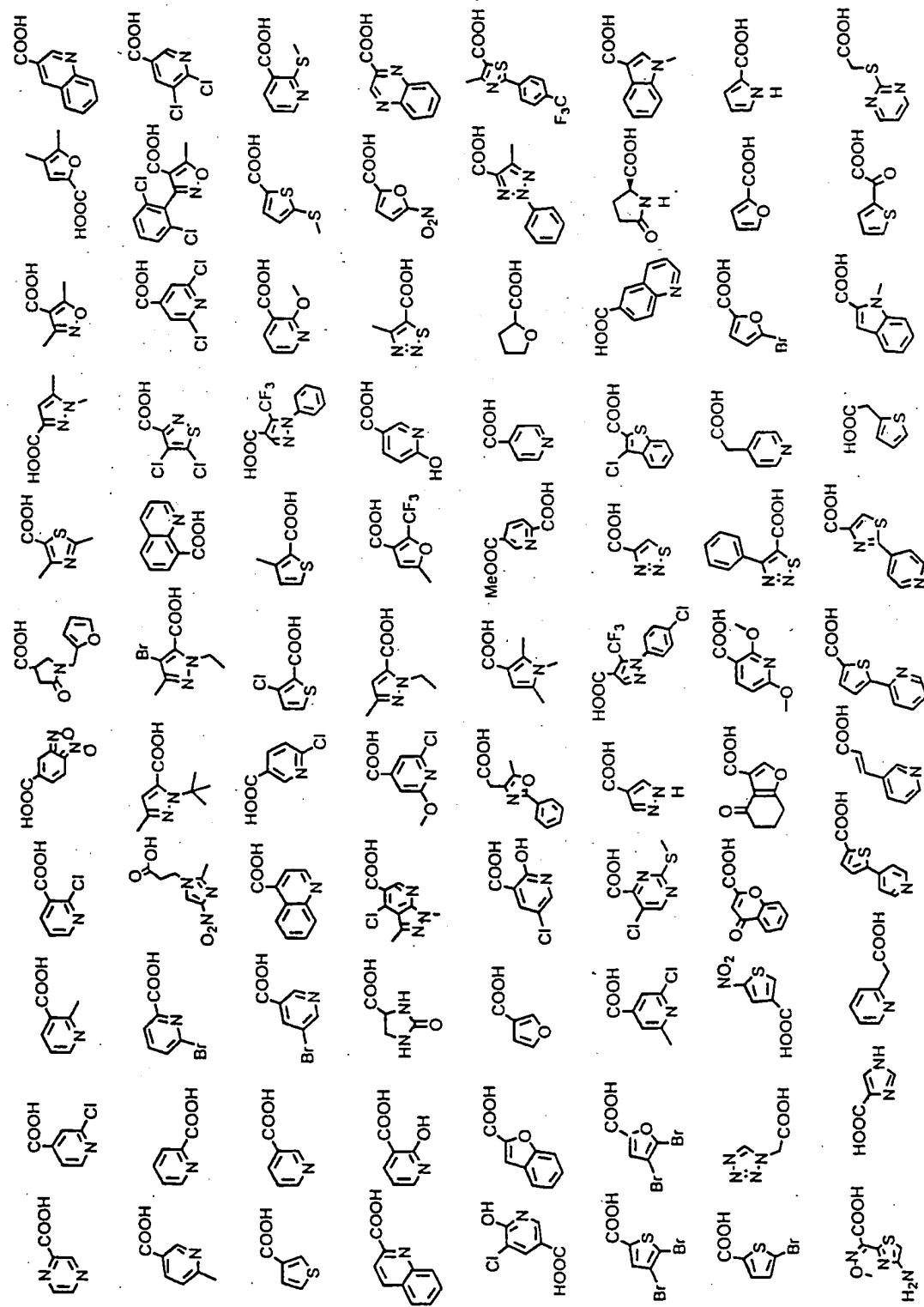


FIGURE 42

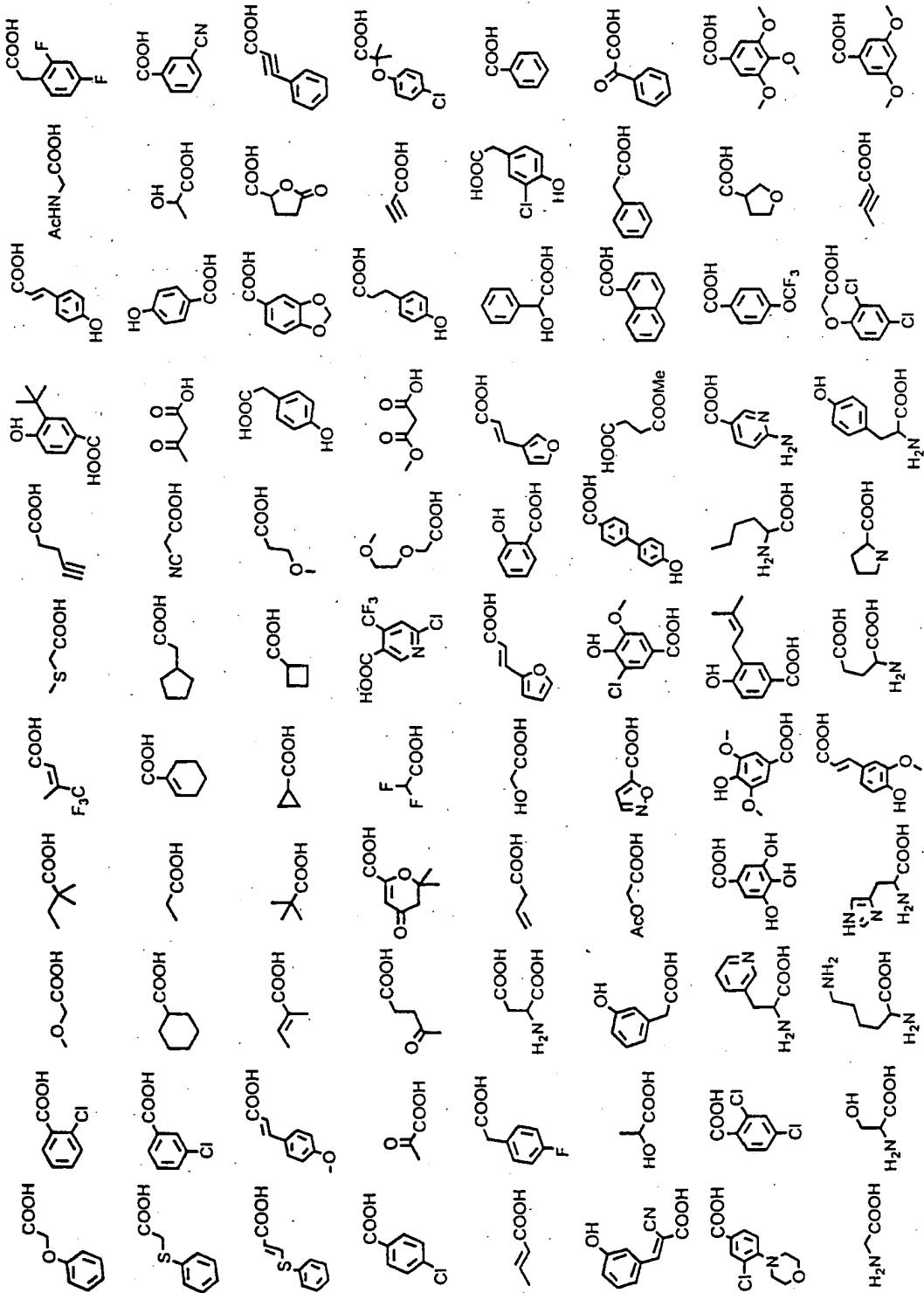


FIGURE 43

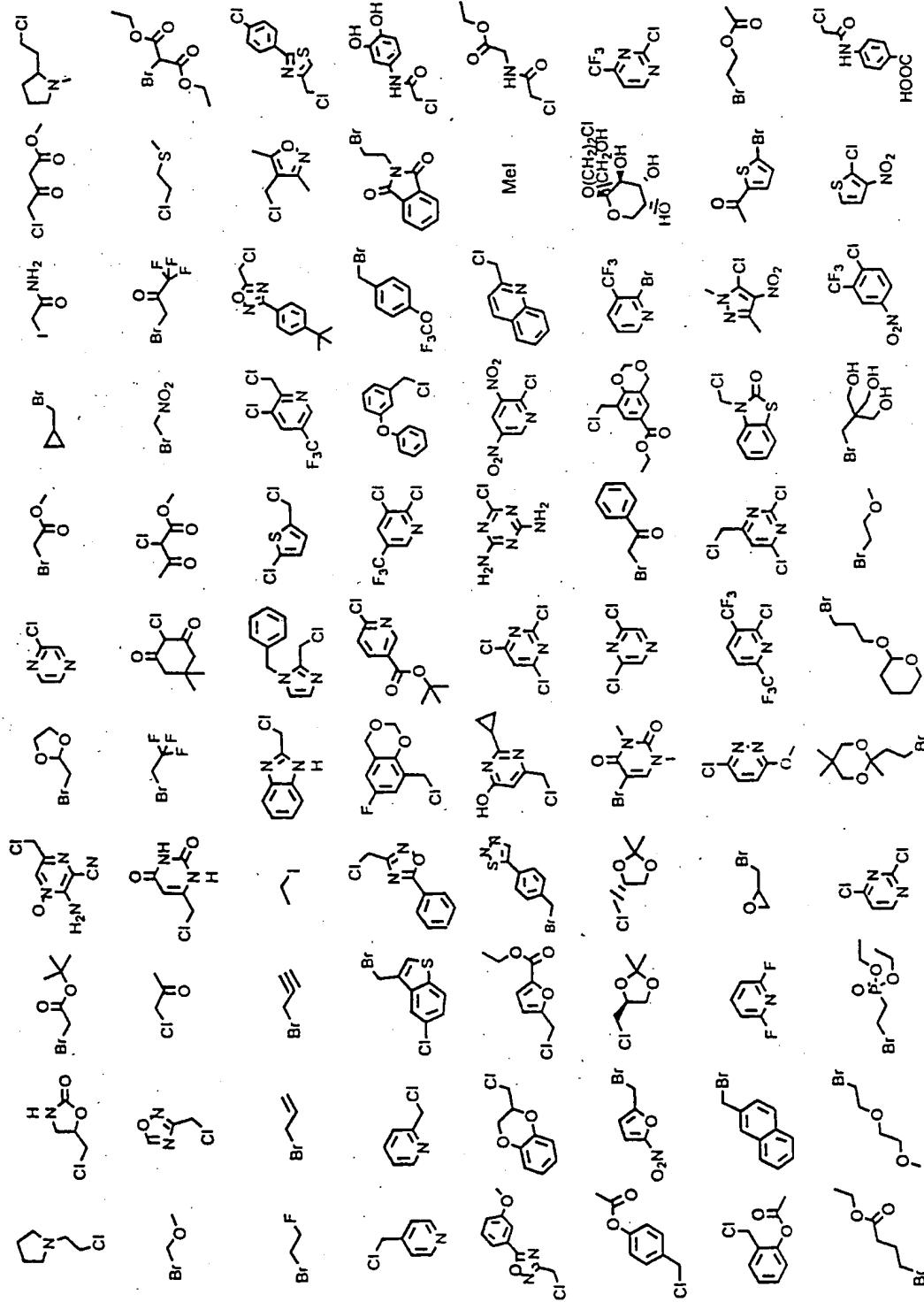


FIGURE 44

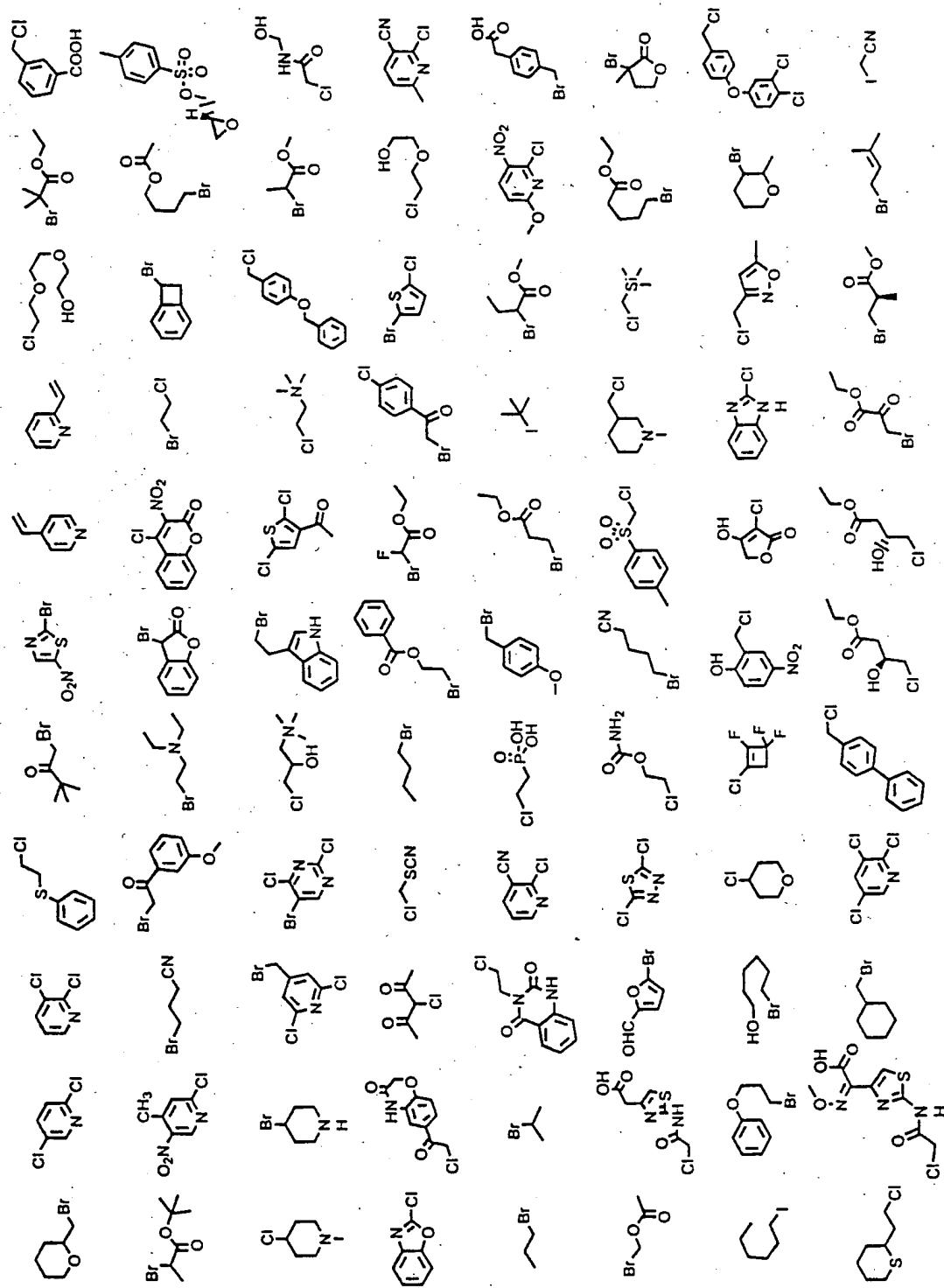


FIGURE 45

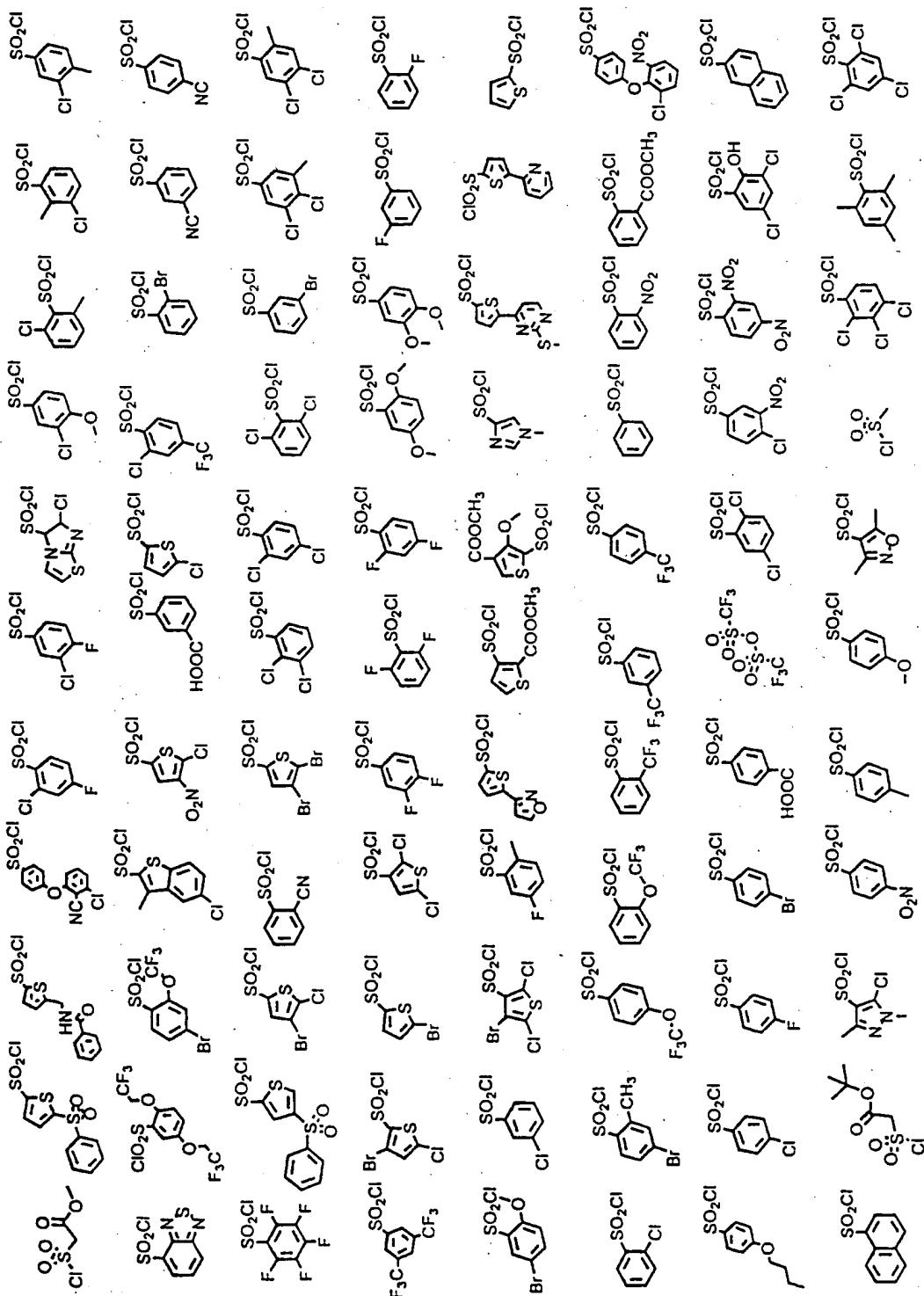


FIGURE 46

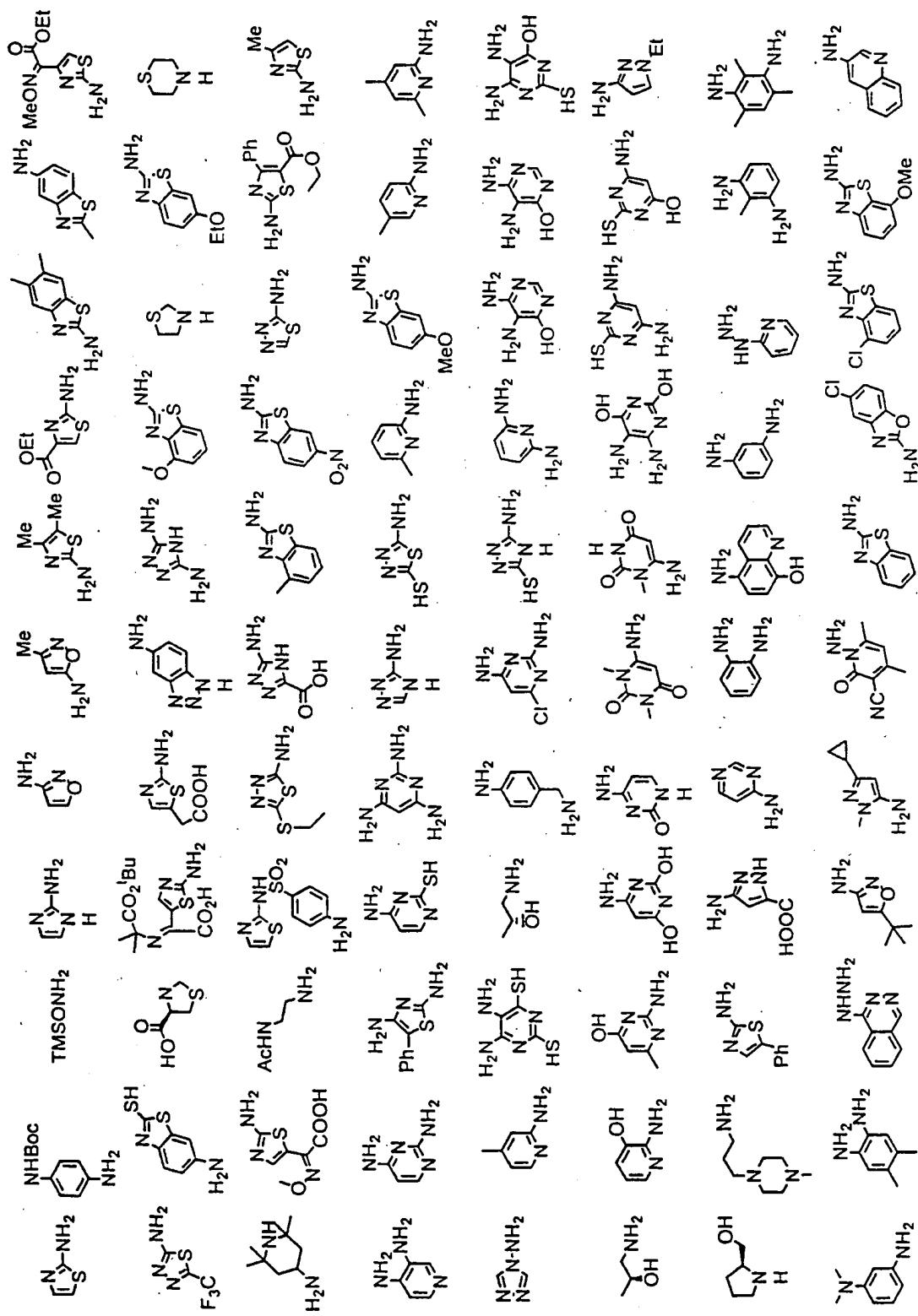


FIGURE 47

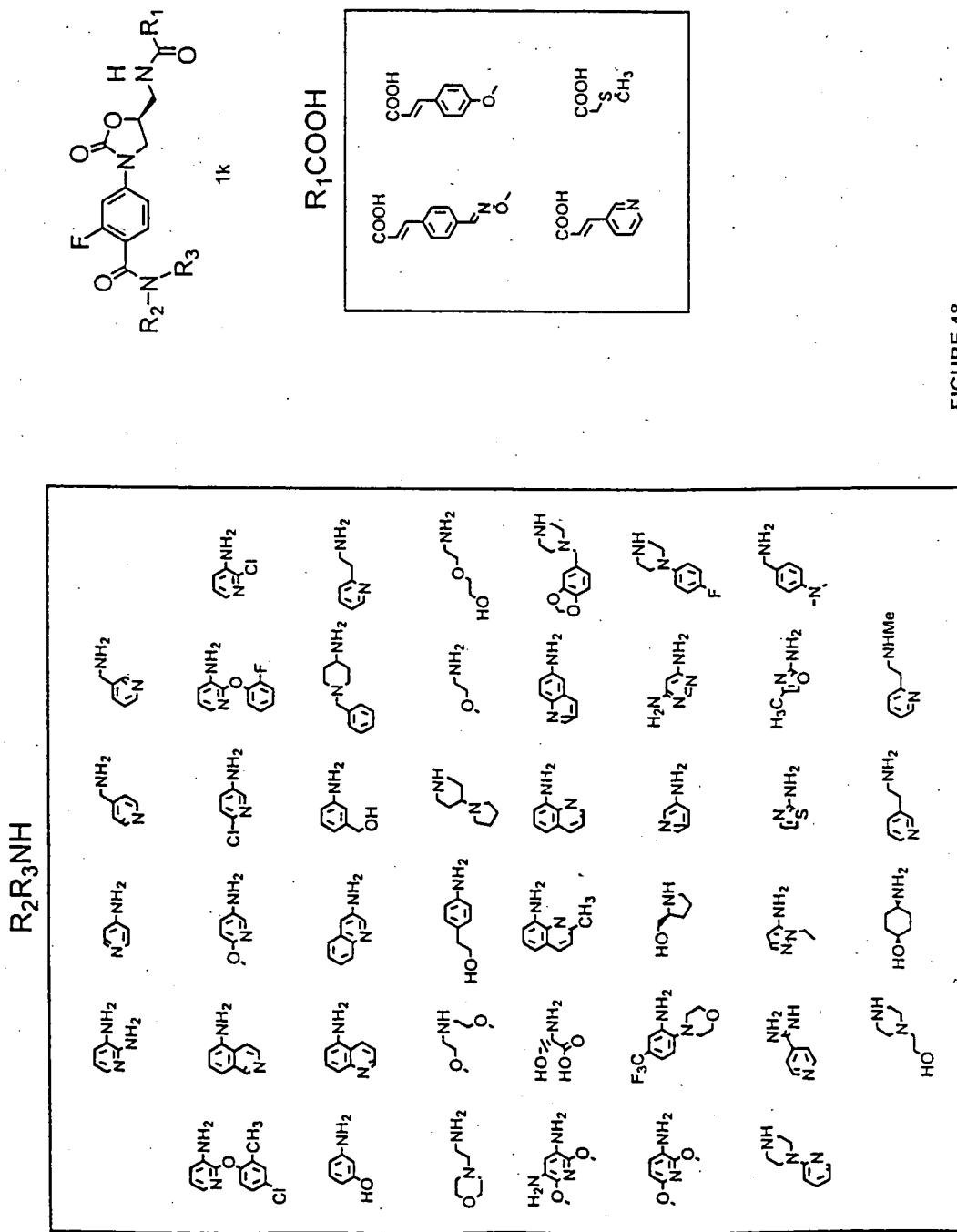


FIGURE 48

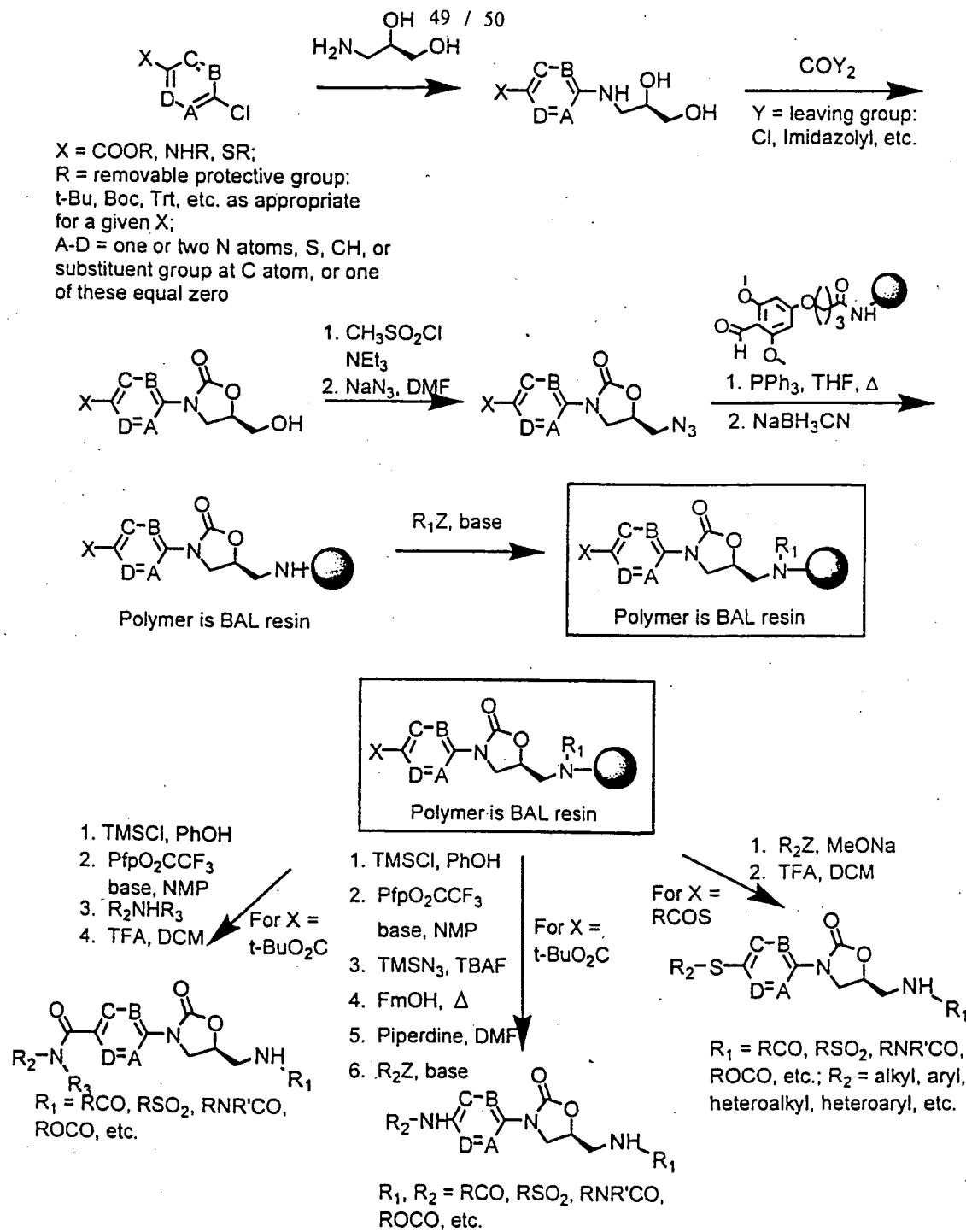
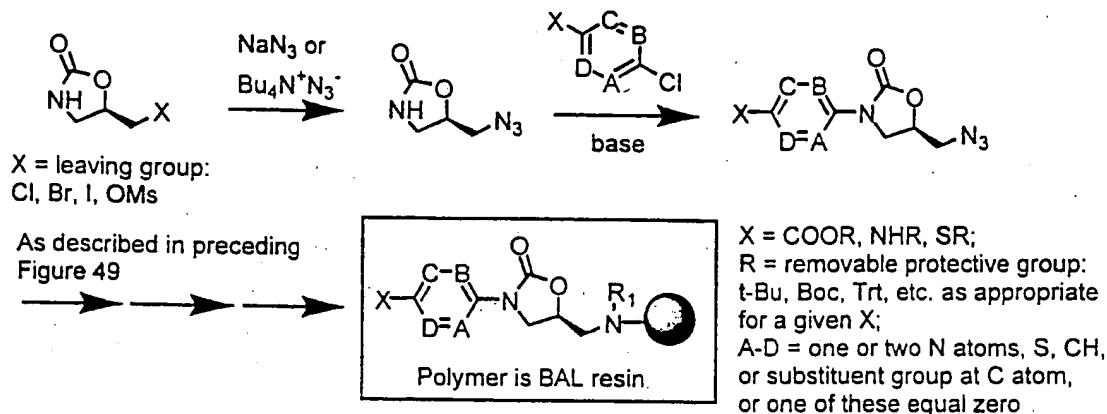


FIGURE 49

Synthesis from 5-(S)-azidomethyloxazolidinone



Synthesis from 5-(S)-(protected amino)methyloxazolidinone

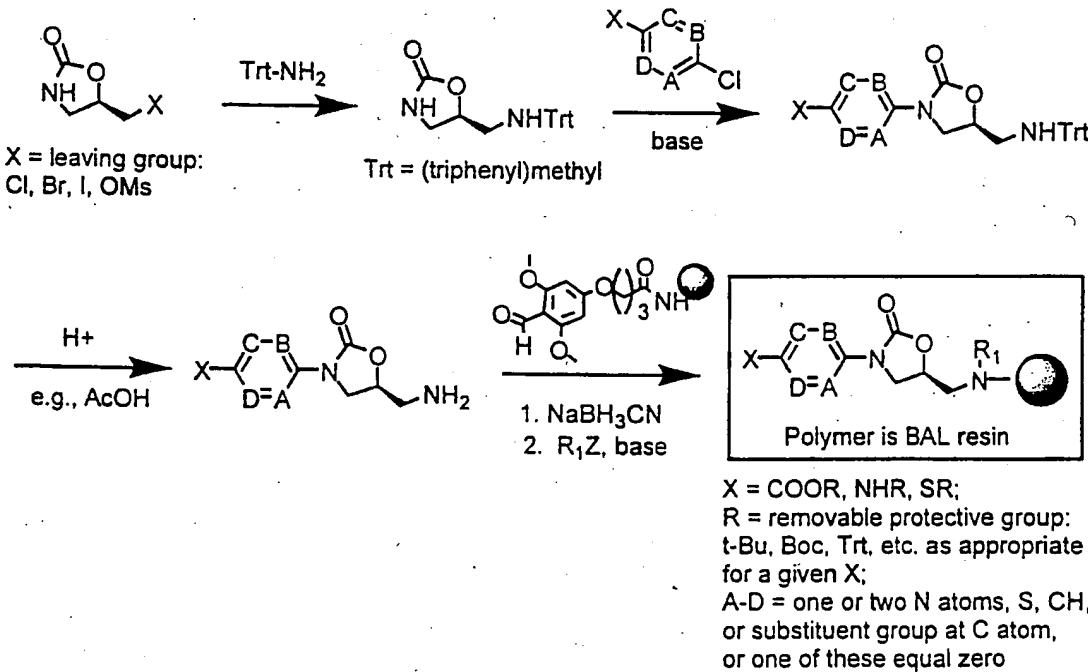


FIGURE 50

INTERNATIONAL SEARCH REPORT

Int'l. Application No
PCT/US 99/01318

A. CLASSIFICATION OF SUBJECT MATTER					
IPC 6 C07D263/20	C07D413/12	C07D417/12	C07F9/653	C07D417/04	C07D413/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07D C07B A61K C07F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 30981 A (PHARMACIA & UPJOHN CO) 28 August 1997 see claims	7-9, 13-43, 60-82, 95
X	WO 97 21708 A (PHARMACIA & UPJOHN CO) 19 June 1997 see claims	7-9, 13-43, 60-82, 95
X	WO 98 01446 A (ZENECA LTD) 15 January 1998 see claims	7-9, 13-43, 60-82, 95
		-/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the International search	Date of mailing of the international search report
21 April 1999	03/05/1999
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl. Fax: (+31-70) 340-3016	Authorized officer Henry, J

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/01318

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 01447 A (ZENECA LIMITED) 15 January 1998 see claims ---	7-9, 13-43, 60-82,95
X	WO 95 14684 A (UPJOHN CO) 1 June 1995 see claims ---	7-9, 13-43, 60-82,95
X	US 4 801 600 A (WANG CHIA-LIN J ET AL) 31 January 1989 see claims ---	7-9, 13-43, 60-82,95
X	WO 93 09103 A (UPJOHN CO) 13 May 1993 see claims ---	7-9, 13-43, 60-82,95
X	WO 93 23384 A (UPJOHN CO.) 25 November 1993 see claims ---	7-9, 13-43, 60-82,95
X	WO 94 13649 A (UPJOHN CO) 23 June 1994 see claims ---	7-9, 13-43, 60-82,95
X	WO 95 07271 A (UPJOHN CO) 16 March 1995 see claims ---	7-9, 13-43, 60-82,95
X	WO 97 10223 A (PHARMACIA & UPJOHN CO) 20 March 1997 see claims ---	7-9, 13-43, 60-82,95
X	EP 0 127 902 A (DU PONT DE NEMOURS) 12 December 1984 see claims ---	7-9, 13-43, 60-82,95
X	EP 0 184 170 A (DU PONT DE NEMOURS) 11 June 1986 see claims ---	7-9, 13-43, 60-82,95
X	EP 0 312 000 A (DU PONT DE NEMOURS) 19 April 1989 see claims ---	7-9, 13-43, 60-82,95

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/01318

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 316 594 A (DU PONT DE NEMOURS) 24 May 1989 see claims ---	7-9, 13-43, 60-82,95
X	EP 0 352 781 A (DU PONT DE NEMOURS) 31 January 1990 see claims ---	7-9, 13-43, 60-82,95
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
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Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.:

95-100
because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claims 95-100

are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. Claims Nos.:

because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. Claims Nos.:

because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

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